ABSTRACTS OF WORLD MEDICINE

VOL. 22 No. 3 SEPTEMBER, 1957

Pathology

521. **Derivation of Certain Forms of " Fibrinoid " from Smooth Muscle**

E. E. MUIRHEAD, E. BOOTH, and P. O'B. MONTGOMERY. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] 63, 213–228, March, 1957. 9 figs., 40 refs.

The authors, at the Southwestern Medical School of the University of Texas, have continued their study of the pathogenesis of the " fibrinoid " change of vascular smooth muscle and renal glomeruli. Smooth muscle from the stomach and colon of dogs was allowed to autolyse under sterile conditions for 12 to 24 hours and then blended to form a fine suspension in saline or buffer solution. This material was injected unilaterally into the temporarily clamped renal arteries of anaesthetized dogs. The kidneys, when removed for examination 12 to 24 hours later, showed multiple infarcts, with injected material in the intertubular arteries and glomerular vessels as well as in some tubules.

The histochemical reactions of autolysed muscle were compared, in sections of these kidneys and *in vitro*, with fibrinoid in kidney sections from human cases of hypertension. Both materials were coloured red with Mallory's and Masson's trichrome stains, yellow with the Van Gieson stain, purple with the phosphotungstic-acid–haematoxylin agent, and blue with Weigert's fibrin stain. Both were sudanophil and gave positive reactions in the free potassium, free carbonyl, and protein-bound sulphhydryl procedures. Human fibrinoid gave a positive reaction to the periodic-acid–Schiff test, but autolysed muscle gave a positive reaction only *in vitro* or in frozen section, the response being negative in paraffin sections.

The similarity in staining reactions is considered to support the authors' hypothesis that fibrinoid is derived from smooth muscle. In the human cases it was sometimes seen that glomerular fibrinoid was continuous with that of the afferent arteriole, and it is suggested that fibrinoid travels along the vessel lumen to be deposited in the glomerulus. *M. C. Berenbaum*

522. **The Comparative Vascularity of Cutaneous Xanthomas and Atheromatous Plaques of Arteries**

S. L. WILENS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 4–9, Jan., 1957. 2 refs.

Since both cutaneous xanthomata and atheromatous plaques of arteries contain a large amount of lipid rich in cholesterol it has been suggested that the two lesions may be somewhat analogous. An investigation was undertaken at the New York University College of Medicine to determine whether histological analysis would reveal how clearly these two types of lesion can be related on anatomical grounds. Considerable differences in the structural evolution of these lesions were found. (1) Their age and sex distribution are different. (2) A striking difference exists in the size that aggregates of fat cells can achieve in the two lesions: intact " foam " cells occupying areas more than 1 cm. in diameter may be found in xanthomata, whereas in arterial plaques of this size the fat-laden cells have invariably disintegrated to form a central atheromatous mass. (3) Another significant difference is in the degree of vascularity encountered: in sharp contrast to atheromatous plaques, cutaneous xanthomata are frequently highly vascularized. Probably as a result of this xanthomata undergo fibrosis more regularly and much more uniformly than do arterial plaques. (4) A moderate degree of hyalinization of connective tissue was present in 19 of 58 xanthomata, but calcification did not occur.

It is considered that the major difference lies in the initial vascularity of the two types of tissue involved.

A. W. H. Foxell

523. **Keratinization of the Duct of the Sebaceous Gland and Growth Cycle of the Hair Follicle in the Histogenesis of Acne in Human Skin**

E. J. VAN SCOTT and R. C. MACCARDLE. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **27**, 405–412, Dec., 1956 [received April, 1957]. 2 figs., 8 refs.

The earliest changes in the structure of the hair follicles and sebaceous glands in acne are not known. In an attempt to elucidate this problem, horizontally cut sections from biopsy material taken from both healthy subjects and patients with acne were studied at the National Cancer Institute, Bethesda, Maryland. The sections were then used to prepare models in balsa wood of the pilo-sebaceous apparatus. In healthy subjects the hair follicles of the beard and scalp were found to be much larger than those of the back. About half the follicles on the back produced two hair roots, whereas all those from the beard and scalp gave rise to one only. In the beard the follicular lumen was divided into two channels, one for the hair and one for the sebum. In early acne the neck of the affected follicle was elongated and dilated. The orifice of the sebaceous gland was dilated and filled with horn; its wall contained a clearly defined granular layer which was absent in normal glands. In the beard the channel leading from the gland to the surface was filled with horny material, but the channel

used by the hair shaft was normal. In later lesions the whole of the lumen of the follicular neck was occluded, and below the occlusion were lymphocytes and polymorphonuclear leucocytes. On the back most of the affected follicles were in the resting (telogen) phase of the hair-growth cycle. It is suggested that products of the sebaceous gland may initiate the hyperkeratosis, and that cyclical changes in hair growth may be related to cyclical qualitative or quantitative changes in the sebum.

E. Lipman Cohen

HAEMATOLOGY

524. **Observations on the Glitter-cell Phenomenon**
L. B. BERMAN, G. E. SCHREINER, and J. O. FEYS. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 989–991, Nov. 22, 1956. 1 fig., 12 refs.

The presence of "glitter cells" (polymorphonuclear leucocytes whose granules show brownian movement) in urinary sediment has long been considered evidence of pyelonephritis and as excluding cystitis. Bearing in mind the increased need for accurate diagnosis of pyelonephritis because of the wider recognition of its aetiological role in a number of conditions, such as hypertension and pregnancy toxaemia, the authors of this paper from Georgetown University Medical Center, Washington, D.C., present certain clinical and laboratory observations concerning the significance of glitter cells in the urine. The supravital stain, compounded of gentian violet and safranine, introduced by Sternheimer and Malbin (*Amer. Heart J.*, 1949, **37**, 678) was used for the recognition of these cells. It was found that, although the brownian movement can easily be seen in unstained preparations with ordinary microscopy and reduced incident light, the Sternheimer–Malbin stain facilitates the recognition of abnormal nuclear-dye absorption and also of other formed elements. It is concluded that glitter cells are damaged polymorphonuclear leucocytes that have found their way into the urine by a variety of routes. Whereas their absence from the sediment on repeated examination is regarded as evidence against pyelonephritis, their presence should arouse suspicion of the disease. A warning note is, however, sounded against over-interpretation of the glitter-cell phenomenon as specific for renal infection.

L. A. Elson

525. **The Mechanism of Clot Retraction and Viscous Change in the Platelets.** (Sur le mécanisme de la rétraction du caillot et de la métamorphose visqueuse des plaquettes)
Y. BOUNAMEAUX. *Revue d'hématologie* [*Rev. Hémat.*] **12**, 16–34, Jan.–March, 1957. 6 figs., 21 refs.

As is well known, clot retraction requires the presence of fibrinogen, thrombin, glucose, and certain other factors in addition to platelets. The adjuvant factors are not specific, and may be any of several organic or inorganic salts which are enumerated. In studies carried out at the University of Zürich the author has shown that clot retraction can be prevented by a number of agents, whose mode of action is discussed here; these include cysteine, "thephorin" (phenindamine hydrogen tartrate), potassium cyanide, sodium fluoride, and methylene blue.

He concludes that it now seems clear the clot retraction is the result of a viscous change in the platelets, while deficient retraction may be the result either of a specific change in the platelets or of a lack of thrombin.

A. Piney

526. **Studies on the Purification of Thromboplastic Plasma Component (Antihemophilic Substance) in Human Blood**
G. Y. SHINOWARA. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 528–537, May, 1957. 6 figs., 20 refs.

CHEMICAL PATHOLOGY

527. **A Quick and Easy Method for Blood-sugar Estimation**
M. H. DAVIES and R. G. PALEY. *British Medical Journal* [*Brit. med. J.*] **1**, 501–502, March 2, 1957. 7 refs.

A rapid method for estimating the blood sugar level which involves the use of two commercially-prepared, standardized tablets is described, Tablet A containing salicylsulphonic acid and Tablet B copper sulphate, sodium hydroxide, sodium bicarbonate, and citric acid. Tablet A is dissolved in 2 ml. of water in a graduated tube; 1 ml. of blood is added to the solution, which, after being shaken, is filtered into a second graduated tube and 1 ml. of filtrate collected. Tablet B is added to the filtrate, which boils without external heat, the resulting colour being compared with a standard colour chart: blue=100 mg. per 100 ml., green=150 mg. per 100 ml., and orange=200 mg. per 100 ml.

Three different workers at the University of Leeds used this method for about 300 estimations, the results being compared with independent estimates of the blood sugar level by the Hagedorn–Jensen method. In none of the specimens of blood given an orange rating was the true blood sugar level less than 160 mg. per 100 ml., and only in one given a blue rating was the true level more than 125 mg. per 100 ml.

It is suggested that the procedure may be useful in an emergency to obtain a rough estimate of the true blood sugar level.

H. Harris

528. **A Rapid Method for the Estimation of Blood Sugar**
R. A. OSBORN. *British Medical Journal* [*Brit. med. J.*] **1**, 502–503, March 2, 1957. 3 refs.

At the Diabetic Clinic of the Middlesex Hospital, London, blood sugar levels were determined by the method described in Abstract 527 and the results compared with those obtained on duplicate blood samples by the method of Kingsley and Reinhold, sodium tungstate and sulphuric acid being used as the protein precipitant. There was reasonable agreement between the results of the two methods, but the author does not consider that the tablet method is "suitable for control of treatment in hospital diabetic clinics, where arrange-

ments can usually be made for blood-sugar estimations by routine methods ". It may be useful, however, where laboratory facilities for accurate estimation are not readily available. *H. Harris*

529. **Radioactive Dilution Indicator. I. Measurement of Residual Fluid in the Fasting Stomach. II. Gastric Analysis**

D. LIEBOWITZ, H. H. STONE, D. LEVINE, K. G. SCOTT, and T. L. ALTHAUSEN. *Gastroenterology* [*Gastroenterology*] **32**, Feb., 1957, 265–257, 1 fig., 1 ref., and 258–278, 2 figs., 12 refs.

The authors describe, from the University of California, Los Angeles, a method for detecting the amount of gastric secretion remaining in the supposedly empty stomach after conventional aspiration by stomach tube. The method involves the administration of a test meal containing the radioactive isotopes of zirconium and niobium (^{95}Zr, ^{95}Nb), which are poorly absorbed in the stomach. The composition of the test meal is: water, 118 ml.; ^{95}Zr–^{95}Nb, 0·5 μc. in 1 ml. water; sodium calciumedetate (a chelating agent preventing adsorption of the isotopes by the gastric mucus), 37·5 mg. in 1 ml. of water. Duplicate 10-ml. samples are taken from this mixture before administration in order to determine radioactivity and hence concentration of ^{95}Zr–^{95}Nb. The meal is given to the patient in the left lateral decubitus position after conventional aspiration and is mixed with the residual gastric contents by withdrawing and readministering the mixture three times through a 100-ml. syringe, after which further samples are taken for determination of isotope concentration. The whole procedure lasts about one minute. The volume of the gastric contents, that is, test meal plus gastric residuum, is given by the formula: $\frac{V_m \times C_m}{C_1}$ where V_m is volume of the test meal, C_m is concentration of the isotopes in the test meal, and C_1 is the isotope concentration in the diluted stomach contents. In tests on 36 patients after complete " blind " aspiration the volume of the gastric residuum was found to range from 3 to 83 ml. (mean 39·2±2·18 ml.). Over 75% of the patients showed a residual volume of 20 ml. or more.

In estimating gastric secretion and emptying two meals are given, the first as above and the second consisting of water, 118 ml.; ^{95}Zr–^{95}Nb, 0·5 μc., and sodium calciumedetate, 37·5 mg., each in 1 ml. water. The procedure is as follows. Complete emptying by tube and estimation of residuum as before (free and total acid estimated from first aspiration); then once a minute during the 15-minute test period the gastric contents are mixed by aspiration and re-injection and duplicate 10-ml. samples removed for determination of radioactivity at end of test period; the second meal is now given, mixed rapidly, and duplicate 10-ml. samples removed for counting. The volume of pyloric emptying, the amount of the fluid left in the stomach at the end of the test, and the volume of gastric secretion are calculated from simple formulae. [The original should be consulted for the mathematics.]

The results by this method are said to compare favourably with those obtained by dye-dilution techniques. The method is not proposed as a substitute for conventional methods of gastric analysis, but it should be useful for a more complete evaluation of the effects of various foods and pharmacological agents on gastric function. *I. M. Rollo*

530. **Histamine Stimulation of Gastric Pepsin Secretion in Man**

B. I. HIRSCHOWITZ, J. L. LONDON, and H. M. POLLARD. *Gastroenterology* [*Gastroenterology*] **32**, 85–87, Jan., 1957. 1 fig., 8 refs.

Evidence in the literature regarding the influence of histamine upon gastric pepsin secretion being rather contradictory, investigations were carried out at the University of Michigan Medical School, Ann Arbor, in an attempt to settle the controversy.

Gastric juice was obtained from fasting human subjects by continuous aspiration through a No. 12 Levin tube placed in the body of the stomach, and was divided into consecutive half-hourly samples. After one hour an intravenous infusion was started and continued to the end of the experiment. Isotonic saline alone was infused in 13 control experiments, and in 27 studies on 23 subjects 8 μg. of histamine base (in 4 ml. of saline) was infused per minute for 2 or (in 11 studies) 3½ hours. To prevent unpleasant side-effects 10 mg. of " benadryl " (diphenhydramine) was added to the infusion and a further 10 mg. given initially intravenously. The free acid and pepsin content of the samples was determined, the latter by the haemoglobin method described by the senior author in a previous paper (*Lancet*, 1953, **1**, 66; *Abstracts of World Medicine*, 1953, **14**, 31) which, in the authors' opinion, is much more reliable than Mett's egg-albumen method.

The results showed that saline infusion alone had no effect on the gastric output of pepsin or hydrochloric acid, whereas the histamine infusion increased the output of pepsin to more than three times the control level in all instances, reaching a plateau after one hour, and had a similarly marked effect on acid secretion. The authors attribute the discrepant results obtained by other workers to inaccuracies in the methods used for pepsin estimation and to differences in the technique of histamine administration.

[If the present findings are confirmed this paper represents a new and important contribution to the physiology of gastric secretion.] *F. S. Freisinger*

531. **A New Method for Measuring Sialic Acid Levels in Serum and Its Application to Rheumatic Fever**

E. L. HESS, A. F. COBURN, R. C. BATES, and P. MURPHY. *Journal of Clinical Investigation* [*J. clin. Invest.*] **36**, 449–455, March, 1957. 4 figs., 26 refs.

Investigations were carried out at the Rheumatic Fever Research Institute, Chicago, into the significance of the colour development in the deproteinized " serum blank " on heating with the sulphuric–acetic acid mixture used in the well-known diphenylamine reaction of Dische for the estimation of sialic acid in glycoprotein complexes.

This colour is also probably due to sialic acid, and estimation after heating with the sulphuric–acetic acid mixture alone, although less sensitive than the diphenylamine method, is simpler [and obviates the "allergic reactions" in many technicians]. Indoles, pyrroles, and tryptophan produce colour with this reagent, but are considered to be removed by protein precipitation with hot 5% trichloracetic acid. The reagent which the authors recommend is one of 5% sulphuric acid and 95% glacial acetic acid heated in a boiling water-bath for 30 minutes. The colour is determined spectrophotometrically at 530 mμ.

The supernatant solution remaining after precipitation of the serum protein with hot 5% trichloracetic acid was dialysed, frozen, and lyophilized, and contained 17% hexoses, 3·5% hexosamine, 13% sialic acid, and 5·8% nitrogen. The colour absorption curves obtained after treatment of this material with the sulphuric–acetic acid and diphenylamine reagents were practically identical with those obtained with pure sialic acid. Serum from healthy subjects gave an optical density of $0{\cdot}265 \pm 0{\cdot}019$ units. Higher levels were found during the "acute phase" of acute rheumatic fever, tuberculosis, and cancer. Serial determinations were made in comparison with the erythrocyte sedimentation rate (Wintrobe) as an expression of rheumatic activity. The raised sialic acid levels were usually 2 weeks later in returning to normal than the E.S.R., and also persisted after the C-reactive protein reaction became negative.

Harry Coke

532. **Serum Enzymes—I. Serum Lactic Dehydrogenase in Myocardial Infarction**

L. P. WHITE. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 984–988, Nov. 22, 1956. 2 figs., 12 refs.

The determination of serum levels of glutamic oxalacetic transaminase (G.O.T.), recently introduced as an aid in the differentiation of myocardial infarction and pulmonary infarction or embolism, suffers from three main defects: (1) abnormal levels of the enzyme persist only for 24 to 72 hours after the infarction occurs; (2) some patients with infarction of limited extent do not show abnormal levels of enzyme; and (3) the method is laborious. As the heart is rich in other enzymes, the practicability of utilizing the serum level of one of these instead of that of G.O.T. has therefore been investigated at Stanford University School of Medicine, San Francisco. The enzymes thus studied were lactic dehydrogenase, aldolase, and hexose isomerase, the serum levels of which were determined and compared with that of G.O.T. in 50 patients in whom the diagnosis of myocardial infarction was under consideration.

It was found that the serum level of lactic dehydrogenase was a good, if non-specific, index of the presence of myocardial infarction. Serum G.O.T. determination on the other hand appeared to be of little use in differentiating myocardial infarction, but was of help in the diagnosis of hepatitis. The superiority of lactic dehydrogenase determination depends on the simplicity of assay and on the greater degree and longer duration of the rise in level of this enzyme in the serum. Lactic dehydrogenase, in common with many other enzymes, is widely distributed throughout the body, and in addition to the myocardium, tissues such as skeletal muscle, liver, kidney, brain, and many tumours contain considerable amounts. Any cause of tissue destruction, such as infection, trauma, or infarction, may be associated with abnormal elevation of serum enzyme levels; the serum level of lactic dehydrogenase may also be raised during pregnancy. If other causes for an abnormal serum enzyme level can be excluded, however, such abnormality may indicate the presence of myocardial infarction. It is suggested that by measurement of serum lactic dehydrogenase the diagnosis of myocardial infarction may occasionally be made in cases in which this diagnosis can be achieved by no other means.

L. A. Elson

533. **The Zinc Sulfate Turbidity Test**

T. E. WILSON, C. H. BROWN, and A. HAINLINE. *Gastroenterology* [*Gastroenterology*] **32**, 483–493, March, 1957. 6 figs., 16 refs.

Comparison of the results of the zinc sulphate turbidity (Z.S.T.) test with the electrophoretic protein patterns as determined by the Tiselius method on 174 serum samples at the Cleveland Clinic Foundation, Cleveland, Ohio, has led to the conclusion that the Z.S.T. test provides a useful and rapid method for determining the γ-globulin content of serum (correlation coefficient 0·59). Z.S.T. appears to be unaffected by serum albumin and α- and β-globulin levels, but is affected by albumin–γ-globulin and total albumin–globulin ratios. A comparison of Z.S.T. test results with clinical diagnoses in 1,187 cases—392 with no evidence of organic disease, 494 of non-infectious, non-hepatic disease, 179 of cirrhosis, 54 of hepatitis, 42 of obstructive jaundice, 12 of infectious disease, and 14 of metastatic hepatic disease—showed the test to be a valuable aid in the diagnosis of hepatobiliary disease, being of most value in the diagnosis of cirrhosis.

The authors found that Z.S.T. values were raised in some cases of hepatitis, higher figures being obtained in chronic than in acute hepatitis. In cases of long-standing jaundice normal Z.S.T. values indicate biliary obstruction, and high values hepatocellular disease. The mean Z.S.T. value in obstructive jaundice is no lower than that in health. The test is not specific for hepatic disease, since any disease affecting the serum γ-globulin level will produce abnormal Z.S.T. values. The significance of low Z.S.T. values in 14 cases is discussed. Low values were most frequently observed in severe renal disease with proteinuria, malignant hypertension, and metastatic carcinoma.

J. E. Page

534. **The Relationship of Serum Sodium to Total Serum Osmolarity: a Method of Distinguishing Hyponatremic States**

E. G. OLMSTEAD and D. A. ROTH. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 392–399, April, 1957. 5 refs.

Microbiology and Parasitology

535. **The Aetiology of Abacterial Meningitis (Results of a Virological Investigation of the Meningitis Epidemic of Summer and Autumn, 1956).** (Zur Ätiologie der abakteriellen Meningitis (Ergebnisse einer virologischen Untersuchung der Meningitisepidemien im Sommer und Herbst 1956))
H. LENNARTZ, G. MAASS, and G. KERSTING. *Klinische Wochenschrift* [*Klin. Wschr.*] **35**, 327–334, April 1, 1957. 12 figs., 36 refs.

After discussing the viral aetiology of aseptic meningitis the authors describe the investigations carried out on material submitted to the laboratory of the Foundation for Poliomyelitis Research, Hamburg, during an epidemic of viral meningitis which occurred in Germany during the summer and autumn of 1956. The clinical features of the cases were similar to those which have been reported in Great Britain and elsewhere, and consisted notably in an acute febrile meningitis, often accompanied by a morbilliform rash and in some cases by moderate cervical lymph-node enlargement. Children were principally affected, and in the cerebrospinal fluid a pleocytosis of up to 10,000 cells per c.mm. was observed.

By means of monkey kidney tissue cultures a virus was isolated from the faeces on 78 occasions, from the cerebrospinal fluid on 36, from the throat once, and from the blood also on a single occasion. The virus showed the biological properties of Coxsackie Group-A virus, but was serologically identical with ECHO virus Type 9. The strain of virus, designated the Magdeburg strain, was shown to be similar to that isolated in Great Britain, Canada, and Italy from similar cases. On re-examination of material from sporadic cases of aseptic meningitis occurring in Germany during the preceding 3 years the authors were able to show that the virus had been present during those years in areas in which the 1956 outbreaks occurred.

[This account suffers from being rather too general and lacks useful details.] *J. E. M. Whitehead*

536. **Contribution to the Taxonomical Classification of the So-called *Pneumocystis carinii*.** [In English]
A. CSILLAG. *Acta microbiologica Academiae scientiarum Hungaricae* [*Acta microbiol.* (*Bp.*)] **4**, 1–8, 1957. 1 fig., 34 refs.

It is now almost universally accepted that *Pneumocystis carinii*, the organism identified by Vanék and Jirovec in the lungs of infants who died of infantile interstitial plasma-cell pneumonia, is the causative organism of this disease. The taxonomic classification of this organism is, however, a matter of controversy. Jirovec and others consider that it is a protozoon, probably a *Holosporidium*, while other workers, particularly Giese, believe that it is a fungus. The present author has previously reported the successful growth of a *Saccharomyces* from the lungs of infants dying of *Pneumocystis* pneumonia which produced in mice structures resembling the octosporous forms of *Pneumocystis carinii*. He now reports, from the State Institute of Hygiene, Budapest, the successful culture of this *Saccharomyces* on media containing ACTH and penicillin in which, after 30 days, octosporous forms were seen. Similar, slightly larger, forms were seen in cultures of *Candida tropicalis*. In a single experiment he obtained a typical ascus-staining fungus.

The author concludes that *Pneumocystis carinii* is a fungus of the *Blastomyces* group, and that several related blastomycetes may be responsible for the disease in infants. The frothy, honeycomb-like masses seen post mortem in the lungs of infants are considered to be empty cell walls from which the cytoplasm has been dissolved. *H. S. Baar*

BACTERIA

537. **Delayed Positive Culture of Tubercle Bacilli: Its Relation to Isoniazid Resistance.** (Positivation tardive de cultures de bacilles tuberculeux: ses rapports avec l'isoniazido-résistance)
G. CANETTI and J. GROSSET. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **20**, 1053–1061, Dec., 1956 [received March, 1957]. 11 refs.

Material from 468 patients with pulmonary tuberculosis undergoing chemotherapy [nature unspecified] was cultured at the Institut Pasteur, Paris, for the tubercle bacillus, 5 tubes of Loewenstein–Jensen medium being used for each specimen. Of 1,468 cultures made, 542 (37%) were positive (colonies visible to the naked eye) within 133 days. Of these, 432 (79·7%) were positive within 30 days, 94 (17·3%) within 60 days, 10 (1·8%) within 80 days, and 6 (1·2%) only after more than 80 days. Colonies appearing after 60 days or more (delayed cultures) were typical in appearance of the human variety of tubercle bacillus, but in 14 out of 15 such cultures on which counts were made there were no more than 10 colonies per tube, the lower numbers being associated with a later date of appearance. In contrast, 371 of 526 cultures positive within 60 days had more than 10 colonies and only 37 fewer than one colony per tube.

Isoniazid and streptomycin sensitivity was studied in a total of 500 cultures positive within 60 days and in 14 delayed cultures. No differences were found between the two groups in their behaviour to streptomycin. With isoniazid, however, 273 cultures were resistant (growing in the presence of 1 to 25 μg. per 17-mm. tube), of which 13 (4·8%) were delayed cultures, and 241 were sensitive (not growing in the presence of 1 μg. or more per tube), of which only one (0·4%) was a delayed

culture. Of cultures with 1 to 10 colonies per tube, 9% of the isoniazid-resistant and 1·4% of the isoniazid-sensitive organisms were from delayed cultures. However, when there was less than one colony per tube the respective figures were 47% and *nil*. The delayed appearance of positive cultures is thus considered to be associated with isoniazid resistance and scanty colony formation. *M. Lubran*

538. **The Pathogenicity of Atypical Chromogenic Mycobacteria for the Rhesus Monkey**
L. H. SCHMIDT, R. HOFFMANN, and W. STEENKEN. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **75**, 169–179, Feb., 1957. 4 figs., 14 refs.

This paper from the Christ Hospital Institute of Medical Research, Cincinnati, Ohio, and the Trudeau Foundation, New York, describes an attempt to infect rhesus monkeys with two strains of chromogenic mycobacterium recovered from cases of human infection and described by Wolinsky *et al.* [see Abstract 539]. Each strain was inoculated intratracheally into a group of 8 healthy monkeys in pairs at dilutions of 10, 10^{-2}, 10^{-4}, and 10^{-6}; the animals were examined radiographically 2, 4, 8, and 12 weeks after infection, and measurements of hypersensitivity to old tuberculin were also made. After 91 days the surviving monkeys were killed and examined post mortem. In each series only the pair of animals inoculated with the heaviest concentration of organisms (more than 10^7 viable units) showed any evidence of disease, and in 3 out of these 4 the disease was undergoing healing. The fourth monkey died with a caseous pneumonia which was confined to one lobe. Tuberculin hypersensitivity of a low order and of short duration was produced by both strains of mycobacterium.

The general picture was less severe than that produced by virulent human tubercle bacilli, but more severe than that produced by avirulent or attenuated strains such as H37Ra or BCG. It is suggested that the ability of such atypical acid-fast bacilli to produce disease is governed by the susceptibility of the host rather than the virulence of the organism. *John M. Talbot*

539. **Atypical Chromogenic Mycobacteria Associated with Pulmonary Disease. Including a Report of Three Cases**
E. WOLINSKY, M. M. SMITH, R. S. MITCHELL, and W. STEENKEN. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **75**, 180–198, Feb., 1957. 5 figs., 35 refs.

Three cases of human infection with chromogenic acid-fast bacilli are reported from the Trudeau Foundation, Saranac Lake, New York. All 3 patients gave a history suggestive of active tuberculous infection and showed a radiographic appearance of chronic disease with cavitation; this did not respond to chemotherapy, and resection of the affected area was undertaken. In each case chromogenic acid-fast bacilli were recovered from the sputum before operation. The strains were non-pathogenic to guinea-pigs, non-cord-forming, catalase positive, and neutral-red negative; they had a slightly increased resistance to streptomycin and isoniazid and a moderately increased resistance to PAS *in vitro*, as compared with the standard H37Rv strain of tubercle bacillus. All three strains were avirulent for guinea-pigs on intramuscular injection, the animals showing a transient weak tuberculous hypersensitivity; the patients all gave a positive tuberculin reaction at dilutions between 1 in 10,000 and 1 in 100. The following possible origins of these strains are discussed: (1) that they are naturally attenuated variants of *M. tuberculosis*; (2) that they are variants attenuated by chemotherapy; (3) that they are saprophytic mycobacteria colonizing old tuberculous lesions; (4) that they are variants of mammalian tubercle bacilli. None of these theories, however, gives an entirely satisfactory explanation.

Results of injection of 2 of the strains into rhesus monkeys are reported by Schmidt *et al.* [see Abstract 538]. *John M. Talbot*

540. **The Properties of *para*-Aminosalicylic Acid-resistant *Mycobacterium tuberculosis* var. *hominis***
M. TSUKAMURA. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **75**, 608–617, April, 1957. 6 refs.

SEROLOGY AND IMMUNOLOGY

541. **Sarcospores and Toxoplasm Serology. An Investigation of Their Alleged Cross-reaction**
I. A. B. CATHIE and G. W. CECIL. *Lancet* [*Lancet*] **1**, 816–818, April 20, 1957. 5 refs.

At the Hospital for Sick Children, Great Ormond Street, London, the authors have examined the claim of Awad (*Trans. roy. Soc. trop. Med. Hyg.*, 1954, **48**, 337) that sarcospores of *Sarcocystis tenella* can be used interchangeably with *Toxoplasma* in the dye test for the diagnosis of human toxoplasmosis, and have repeated his work.

Fresh sarcospores of *S. tenella* were used in parallel tests with toxoplasms on 23 human sera of known toxoplasm-antibody content. All of these gave a positive result with sarcospores, but only about one-third of them with toxoplasms. A further 93 unselected human sera were then tested, and all were found to contain antibodies which modified the sarcospores and gave a positive result. When the first 23 sera were inactivated at 56° C. for 30 minutes and retested with sarcospores the results became negative. This may have been due to the destruction by heat either of a sarcospore-hostile factor or of the accessory factor essential for the *Toxoplasma* dye test. After the addition to the inactivated sera of accessory factor, in the form of unheated human serum known to be free of *Toxoplasma* dye-test antibody, positive results were again obtained in one-third of them with toxoplasms, showing that the *Toxoplasma* dye-test antibody was still complete. But as all of 116 normal sera tested contained sarcospore-hostile factor, no similar source of accessory factor for retesting these sera with sarcospores was available. A

series of tests carried out with the serum of a guinea-pig immunized with *Sarcocystis* complement-fixing antigen confirmed this finding. Of 10 sheep sera tested at random, 6 contained complement-fixing antibodies for sarcosporidiosis and all 10 gave a positive result in the dye test with sarcospores. After inactivation these sera no longer modified fresh sarcospores, but they did modify old sarcospores to give a positive result—a perplexing and unexplained finding.

The present authors were thus unable to obtain results at all comparable with those of Awad and have found it impossible to use sarcospores for the diagnosis of any disease by means of the dye test. This discrepancy may have been due to their omission of some technical detail not mentioned in Awad's description of his experiments.

F. Hillman

542. **Laboratory and Vaccination Studies with Dried Smallpox Vaccines**

W. C. COCKBURN, R. M. CROSS, A. W. DOWNIE, K. R. DUMBELL, C. KAPLAN, D. McCLEAN, and A. M. M. PAYNE. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **16**, 63–77, 1957. 1 fig., 4 refs.

In a vaccination and laboratory study, two dried smallpox vaccines (designated P and Q) were tested at intervals of 4, 8, 16, and 32 weeks after storage at both 37° C and 45° C. Vaccine P was also tested after 64 weeks at these temperatures and gave 100% successful vaccination rates after all periods of storage at both temperatures. Vaccine Q deteriorated within 4 weeks, rapidly at 45° C and less rapidly, but very substantially, at 37° C. There was no clear evidence of the cause of this deterioration, but there was a suggestion of denaturation of some of the samples stored at the higher temperature. So far as could be ascertained, the laboratory results—rabbit skin scarification tests and chorio-allantoic membrane pock counts—ran parallel with the vaccination success rates. The pock count was found to be the more accurate method of laboratory titration. Vaccine P as used in the trial was not an exceptional batch.

Vaccines which give a pock count of 10^8 infective units per ml. will give the highest possible rate of successful primary vaccinations.—[From the authors' synopsis.]

543. **The Heat Resistance of Dried Smallpox Vaccine**

R. M. CROSS, C. KAPLAN, and D. McCLEAN. *Lancet* [*Lancet*] **1**, 446–448, March 2, 1957. 1 fig., 2 refs.

The advantages of a stable dried smallpox vaccine in which living virus can be preserved for long periods at tropical temperatures are obvious. At the Lister Institute of Preventive Medicine, Elstree, Herts., samples of such a vaccine, which was prepared at the Institute and which is free from contaminating bacteria and tissue debris and is easily reconstituted with 40% glycerol in McIlvaine buffer at *p*H 7·2, were held at temperatures of −10° and of +37° and 45° C. for various periods up to 2 years. They were then tested by titration on chick chorio-allantois, by scarification of rabbit skin, and by vaccination of human volunteers not previously vaccinated. The control was the standard glycerinated vaccine kept at −10° C.

The results showed that even when the dried vaccine had been kept at 45° C. for 2 years it still gave 100% "takes" on vaccination. In a further experiment phials of dried vaccine were immersed in boiling water for up to 2 hours; at the end of this time they still retained a sufficient number of infective units to produce 100% successful vaccination. The authors point out that other batches held at 45° C. were tested on volunteers, so that the heat resistance shown was not peculiar to this one batch. As the result of these tests it can safely be stated that this dried vaccine can be transported and kept anywhere in the tropics for considerable periods without risk of deterioration, so that adequate reserves could be held in those countries against possible epidemics.

[As a matter of interest it should be noted that all the human vaccinations (648 in all) were performed with a single ¼-inch (6·4-mm.) scratch. The boiling-water test described may have implications in relation to the sterilization of smallpox-infected clothing or bedding.]

W. K. Dunscombe

544. **Antigenic Activity of British Poliomyelitis Vaccine**

A REPORT TO THE COMMITTEE ON LABORATORY INVESTIGATIONS OF POLIOMYELITIS OF THE MEDICAL RESEARCH COUNCIL. *British Medical Journal* [*Brit. med. J.*] **1**, 366–368, Feb. 16, 1957. 1 fig., 8 refs.

Out of a total of 200,000 British children who were inoculated against poliomyelitis in 1956, 196 aged from one to 11 years who had no detectable antibody before inoculation were investigated serologically at five centres throughout Britain about 2 weeks after the second inoculation. Inoculation consisted in two intramuscular injections each of 1 ml. given at 3 to 4 weeks' interval. The vaccine was prepared in three batches in the laboratories of a commercial firm from an attenuated Brunhilde (Brunender) strain (Type 1), the MEF-1 strain (Type 2), and the Saukett strain (Type 3). Serial dilutions of the sera in Hanks basic salt solution mixed with an equal volume of Parker 199 solution containing 50 $TCID_{50}$ of each of the above strains of virus were tested against 6- to 8-day-old monkey kidney cell cultures. [One $TCID_{50}$=dose infecting 50% of tissue cultures.] The results are presented in tables and a diagram.

Apart from Manchester, where possibly a regional epidemic increased the titre of antibody to Type-1 strain, the titres in all the areas were of the same order of magnitude, the geometric mean for the whole series being 1:72 for Type 1, 1:282 for Type 2, and 1:101 for Type 3. There were no significant differences between the results with the different batches of vaccine. The same three batches of vaccine and a batch from the U.S.A. were then tested on groups of rhesus monkeys which received three injections at weekly intervals. The vaccines all proved to be of similar antigenic activity in these animals. It is thus demonstrated that the vaccine produced an antibody response in the children and in the monkeys, but it is not yet certain what response is required in the test on monkeys to ensure that a substantial response will be obtained in children.

F. Hillman

Pharmacology

545. **Clinical Trials of 10-(α-Dimethylaminopropionyl)-phenothiazine Methobromide—A. The Inhibitory Effect on the Gastric Secretion by Comparison with Atropine Sulphate, Prantal and Ro 2-3773.** [In English]
J. TOMENIUS. *Acta medica Scandinavica* [*Acta med. scand.*] **157**, 11–22, 1957. 21 figs., 25 refs.

A clinical trial of the quaternary ammonium compound 10-(α-dimethylaminopropionyl)-phenothiazine methobromide (also known as " astra 1470 ") to assess its antisecretory and antispasmodic activity was undertaken at St. Göran's Hospital, Stockholm. In healthy medical students an intramuscular injection of 5 to 20 mg. reduced the amount and the acidity of gastric juice secreted during the first hour after injection and inhibited peristaltic movement of the descending colon. The only side-effect was a temporary dryness of the mouth. The same antisecretory and antiperistaltic effects were obtained after an injection of 0·75 mg. of atropine, but this was associated with very troublesome side-effects in 8 out of 10 subjects. Two other ganglion-blocking drugs, " Ro 2-3773 " and " prantal " (diphenmethacil methylsulphate), which were also tested, were less effective and associated with more side-effects than astra 1470. *Robert Mahler*

546. **Polyacrylic Resin: Effective Hydrophilic Colloid for the Treatment of Constipation**
A. J. GROSSMAN, R. C. BATTERMAN, and P. LEIFER. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **5**, 187–192, Feb., 1957. 11 refs.

547. **The Effect of Chlorpromazine and the Modifying Action of Adrenaline on Human Capillaries.** [In English]
E. DAVIS, L. HALPERN, L. LASZLO, and D. DANA. *Confina neurologica* [*Confin. neurol. (Basel)*] **17**, 10–15, 1957. 6 refs.

While chlorpromazine has been shown to have a vasodilator action, there have been few observations of its effect on the capillaries. At the Ezrat Nashim Mental Hospital, Jerusalem, intramuscular injection of 25 mg. of chlorpromazine caused capillary congestion in all of 13 patients tested. In 10 of the patients blueness was observed, and in 8 there was an increase in blood flow; the blueness was thought to be due to increased oxygen consumption. Refractoriness developed in about 15 days with repeated injections. Subcutaneous injection in 5 patients of 0·25 mg. of adrenaline caused capillary constriction in all 5, blueness in 2, and an increase in blood flow in 4. If the same dose of adrenaline was given within two minutes of an intramuscular injection of 25 mg. of chlorpromazine the adrenaline effect predominated, and congestion was absent; if, however, the dose of adrenaline was delayed for 4 minutes after administration of chlorpromazine then the effect of the latter drug predominated.

[The authors suggest the use of adrenaline and possibly ephedrine as antidotes for patients in whom chlorpromazine induces toxic reactions. Since their own work shows that adrenaline must be given within 2 minutes of the injection of chlorpromazine, it seems unlikely to be of much value.] *P. A. Nasmyth*

548. **Studies on the Effect of Dextran on the Coagulation of Blood.** [In English]
U. JACOBAEUS. *Acta medica Scandinavica* [*Acta med. scand.*] **157**, Suppl. 322, 1–103, 1957. Bibliography.

549. **Barbiturate Antagonists to Shorten Drowsiness after Sedated B.M.R. Determinations**
H. K. IBBERTSON, G. F. JOPLIN, and R. FRASER. *British Medical Journal* [*Brit. med. J.*] **1**, 928–930, April 20, 1957. 1 fig., 9 refs.

Although barbiturate sedation facilitates accurate determination of the basal metabolic rate, persisting drowsiness is a disadvantage. At the Postgraduate Medical School of London the effect of the barbiturate antagonist bemegride (β-ethyl-β-methylglutarimide) has been studied in 13 patients previously sedated with up to 9 gr. (600 mg.) of sodium amylobarbitone. Compared with the effect of a saline placebo two oral doses of 150 mg. of bemegride in a 0·5% solution, given at intervals of half an hour, significantly shortened the duration of sedation. The duration of sleep was reduced by an average of 135 minutes, and persistence of incoherent speech and disturbances of gait by 111 and 192 minutes respectively. An over-all incidence of side-effects of 15% was noted; these included mild nausea, mental agitation, and erythematous skin rashes. Bemegride is considered a help in counteracting the unwanted side-effects of barbiturate sedation following estimation of the basal metabolic rate and similar investigations, and other applications are suggested.
Kenneth Gurling

550. **Effect of Morphine and *n*-Allylnormorphine on Cerebral Hemodynamics and Oxygen Metabolism**
J. H. MOYER, R. PONTIUS, G. MORRIS, and R. HERSHBERGER. *Circulation* [*Circulation (N.Y.)*] **15**, 379–384, March, 1957. 10 refs.

The response of the cerebral circulation to large doses of morphine, and its modification by the subsequent administration of the antagonistic drug *n*-allylnormorphine, have been studied in 7 healthy male subjects (aged 17 to 42 years) at Baylor University College of Medicine, Houston, Texas. Cerebral blood flow was measured by the nitrous oxide method before and 10 to 35 minutes after 60 mg. of morphine sulphate had been administered intravenously over 10 minutes. *n*-Allylnormorphine, 25 mg., was then given intravenously, and the observations were repeated 10 to 15 minutes later.

Morphine produced a striking depression of cerebral oxygen consumption (mean change from 3·2 to 1·9 c.cm. per 100 g. of brain per minute; $P<0.01$). Measurements of arterial–cerebral venous oxygen difference made between the flow estimations indicated that the depressant effect appeared 10 to 15 minutes after administration and reached a maximum at between 20 and 30 minutes. *n*-Allylnormorphine produced a rapid reversal of this change and a rise in the mean value for oxygen consumption to 2·5 c.cm. per 100 g. of brain per minute ($P<0.05$); in 4 instances control values were restored. Thus morphine appears to have no direct effect on cerebral blood vessels, although the changes in arterial gas tensions (rise in pCO_2, fall in pO_2) associated with its respiratory depressant action tend to lower cerebral vascular resistance and hence to augment cerebral blood flow. *S. G. Owen*

551. **Pharmacology of Ethyl-1-(4-aminophenethyl)-4-phenyl*iso*nipecotate, Anileridine, a New Potent Synthetic Analgesic**

L. D. Orahovats, E. G. Lehman, and E. W. Chapin. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **119**, 26–34, Jan., 1957. 3 figs., 10 refs.

At the Merck Institute for Therapeutic Research, Rahway, New Jersey, the authors have investigated a new analgesic, " anileridine ". This drug is a piperidine derivative in which the N-methyl group of pethidine is replaced by an N-(*p*-aminophenethyl) group. In rats the analgesic dose–response curve after subcutaneous injection was similar to that of morphine and showed that anileridine has 12 times the potency of pethidine. The analgesia produced was prompt in onset and reached its maximum in 20 to 30 minutes. The drug was also highly effective by mouth. In tests on dogs anileridine was found to be equipotent with morphine up to 30 minutes, but after this time it became progressively less potent in comparison. In dogs also the new analgesic was highly effective by mouth.

The effect on respiration was measured in cats and dogs anaesthetized with pentobarbitone. It was found that in equal dosage by weight morphine produced a more profound and prolonged depression of both respiratory rate and minute volume than anileridine, while pethidine in equal dosage produced a similar degree of depression to anileridine. In anaesthetized cats and dogs 3 mg. of anileridine per kg. body weight caused a moderate bradycardia and a gradual fall in blood pressure which lasted for 30 to 60 minutes. A similar degree of bradycardia with a more profound fall in blood pressure occurred with this dosage of pethidine, while the same dose of morphine caused marked bradycardia and a greater fall in blood pressure, which lasted for over 2 hours. In further experiments anileridine was found to have considerable antispasmodic, antitussive, and antihistaminic activity. Side-effects such as nausea, vomiting, and constipation were found to be very much less marked than with morphine. In rats and rabbits the new drug was considerably less toxic than pethidine in equipotent dosage. Prolonged administration of the analgesic to rats and dogs showed that anileridine is well tolerated. The analgesic and side-effects of the new drug could be effectively reversed by *n*-allylnormorphine (nalorphine). *Mark Swerdlow*

552. **The Effects of Narcotic Analgetics and Narcotic Antagonists on Respiration**

F. F. Foldes, F. J. Zeedick, and L. R. Koukal. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 153–161, Feb., 1957. 15 figs., 7 refs.

In a study at the Mercy Hospital and the University School of Medicine, Pittsburgh, Pennsylvania, pulmonary ventilation was measured in 110 patients who had received various sequences of the narcotics meperidine (pethidine) or alphaprodine and the antidotes levallorphan or nalorphine at varying intervals. Observations were made of the pulse rate and blood pressure and of the state of consciousness. Equianalgesic doses of the two narcotics produced severe respiratory depression which could be reversed with either of the two antidotes, or largely prevented by their previous administration. Levallorphan premixed with pethidine was equally effective in preventing undue respiratory depression. *Ronald Woolmer*

553. **The Diuretic Activity of a New Pyrimidinedione Administered Orally to Nonedematous Adults**

M. L. Clark and J. A. Hagans. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **49**, 395–400, March, 1957. 1 fig., 6 refs.

The effect of a new oral diuretic drug, " rolicton " (amino*iso*metradine; 1-methallyl-3-methyl-6-aminotetrahydropyrimidinedione), was observed in 23 healthy male subjects at the University of Oklahoma and Veterans Administration Hospital, Oklahoma City. It is suggested that non-oedematous individuals provide a more stable and homogeneous base-line for a comparative study than do oedematous patients [although various abnormal mechanisms are operative in oedematous subjects which may influence the action of a diuretic drug]. A total of 43 tests were carried out, each lasting a week. The subject was confined to hospital in a fairly stable environmental temperature, and " base-line data " were collected during the first 3 days; on each of the next 3 days he was given placebo tablets, or amino*iso*metradine in a dose of 0·4 or 0·8 g. thrice daily with meals, or aminometradine (" mictine "), 0·4 g. thrice daily, the latter being a diuretic of known effect. The 7th day of the test served as a second control period.

Amino*iso*metradine (1·2 g. daily) and aminometradine (1·2 g. daily) produced a significant diuresis and a fall in body weight, with no significant alteration in the specific gravity of the 24-hour specimen of urine. The double dose of amino*iso*metradine produced a marked diuresis on the first day of medication only, and the fall in body weight was maintained for the 3 days of treatment. The placebo produced no significant effects. Side-effects occurred only in the group receiving aminometradine, where 7 of the 9 subjects complained of anorexia and nausea.

It is concluded that amino*iso*metradine is comparable in potency to aminometradine. *T. B. Begg*

Chemotherapy

554. **The Superiority of a Triple Sulfonamide Preparation in Producing High Spinal Fluid Concentrations in Meningitis**

J. M. Beck and A. I. Braude. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] 3, 454–457, Dec., 1956.

An investigation to evaluate the ability of the sulphonamides to cross the blood–brain barrier and to concentrate in the cerebrospinal fluid was carried out at the Parkland Memorial Hospital, Dallas, Texas, on 17 patients, some of whom had meningitis. It was found that a preparation containing equal parts of sulphadiazine, sulphamerazine, and sulphadimidine produced a higher blood sulphonamide level after oral administration than an equal or larger dose of sulphafurazole. In 15 of the 17 patients the ratio of the concentration of sulphonamide in the cerebrospinal fluid to that in the blood was significantly higher for the triple sulphonamide mixture. With both drugs the penetration of sulphonamide into the cerebrospinal fluid was higher in the presence of central nervous system infection.

E. G. Rees

555. **Evaluation of Sulfaethylthiadiazole (SETO) in Common Infectious States in Children**

J. D. Farquhar. *Journal of Pediatrics* [*J. Pediat.*] **50**, 190–195, Feb., 1957. 2 figs., 10 refs.

Reports of the frequent development of resistance to antibiotics have awakened renewed interest in the sulphonamides. The author has therefore tested a new sulphonamide, sulphaethylthiadiazole (SETD), in his general paediatric practice in Philadelphia on 512 children who suffered from a variety of, mostly minor, infections (three-quarters of the children had simple nasopharyngitis). The drug was administered either in tablet or liquid form (1 grain per lb. (140 mg. per kg.) body weight daily in 4 doses) or in a " sustained-release " suspension (110 mg. per kg. daily in 2 doses). A good clinical response was observed in 97% of the children within 3 days of the commencement of therapy. Toxic complications were infrequent, and consisted mostly of mild diarrhoea. Seven different organisms, mostly pneumococci and non-haemolytic streptococci, were obtained on culture in 198 cases. None were resistant to SETD [details of the tests used are not given] and good bacteriological response was obtained in 196 of these cases. In 68 cases (mainly of otitis media or exudative tonsillitis) SETD treatment was combined with an initial single penicillin injection with good results.

It is concluded that this method of treatment of patients in everyday practice successfully shortens the course of infections and virtually eliminates bacterial complications. The use of a readily soluble, easily absorbed sulphonamide, especially when given in a sustained release suspension, avoids the need to use more potent antibiotics and therefore the development of organisms resistant to antibiotics. It is not claimed that SETD would replace antibiotics in the treatment of major infections. (It is noted in an addendum to the paper that similar satisfactory results were obtained in a further 500 paediatric cases.)

John Lorber

556. **The *in vitro* Effect of Combinations of Antibiotics on Resistant Strains of Bacteria Commonly Found in Urinary Tract Infections**

W. E. Clapper and C. Sun. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] 7, 75–80, Feb., 1957. 8 refs.

Aerobacter aerogenes, *Pseudomonas* spp., *Proteus* spp., and *Streptococcus faecalis* are often encountered in urinary-tract infections, particularly after antibiotic treatment. These organisms are often resistant to all the commonly used chemotherapeutic agents. Most strains of *Pseudomonas* are sensitive to polymyxin, but because of the toxic nature of this drug it is not often used. As a synergistic action between polymyxin and oxytetracycline has been noted against some strains of *Pseudomonas* the effect of the former in combination with both oxytetracycline and tetracycline against several strains of these 4 organisms *in vitro* was studied at the Lovelace Foundation, Albuquerque, New Mexico. It was found that these combinations were not very effective against *Strep. faecalis* and *Proteus*, but some synergistic effect was noted against *A. aerogenes* and *Ps. aeruginosa*. Most extensive tests were carried out with these organisms and this synergistic effect was confirmed, the effects of combinations of penicillin, streptomycin, polymyxin, chloramphenicol, erythromycin, oxytetracycline, tetracycline, and novobiocin being also investigated against the same 4 species of bacteria. It was found that although polymyxin combined with tetracycline or oxytetracycline was effective against most strains of *Ps. aeruginosa*, the combination was bactericidal only against much smaller numbers of *A. aerogenes*, although growth was inhibited in about one-half of the strains tested. A synergistic effect was observed with 36% of 22 strains of *Pseudomonas* and 50% of 16 strains of *A. aerogenes*. When a combination of polymyxin in low concentration with chloramphenicol was used, synergism was observed against more than 80% of the strains in both groups. None of these combinations of polymyxin with other drugs appeared to be effective, however, in controlling the growth of *Proteus* or *Strep. faecalis*. However, synergism was observed between penicillin and chloramphenicol against some strains of *Proteus* and *Strep. faecalis*, and also between dihydrostreptomycin and both novobiocin and penicillin.

All these experiments were carried out *in vitro*, and the authors point out that although the results suggest that certain of the combinations tested might be expected to be clinically useful against infections with the organisms concerned, further investigations with a wider variety of strains would be necessary before predictions of clinical efficacy could be made.

R. F. Jennison

Infectious Diseases

557. **Skin Tests in Sarcoidosis**
K. M. CITRON. *Tubercle* [*Tubercle* (*Lond.*)] **38**, 33–41, Feb., 1957. 47 refs.

In this report from the Brompton Hospital, London, the results of the tuberculin test in sarcoidosis are considered, together with the possible causes of diminished tuberculin sensitivity; the relationship between sarcoidosis and tuberculosis is also discussed. Investigation showed that in sarcoidosis the skin may be insensitive not only to tuberculin, but also to other antigens, such as *Candida albicans*, which give rise to delayed reactions. No reaction to a *Candida albicans* antigen was given by 60% of patients with sarcoidosis compared with 10% of a control group of patients with non-tuberculous chest disorders and with pulmonary tuberculosis. Finally the sarcoid tissue suspension (Kveim) reaction is considered.

The paper contains a full review of the literature on skin tests in sarcoidosis. *S. T. Anning*

558. **Clinical Observations on a New Type of Primary Aseptic Meningo-encephalitis.** (Klinische Beobachtungen über eine neuartige primäre aseptische Meningoenzephalitis)
H. F. VON OLDERSHAUSEN. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **82**, 442–447, March 29, 1957. 3 figs., 16 refs.

The author, working at the Rudolf Virchow Hospital, Berlin, describes clinical observations on 75 patients admitted to that hospital in the summer and autumn of 1956 with what he regards as a "new" disease. The condition was highly infectious, the incubation period being 4 to 14 days, and affected in the main children and adolescents from 12 to 22 years old (range 5 to 55 years). Of the 75 patients studied, 39 were males and 36 females. Most of the cases occurred during July, and some gave a history of contact with similar cases in other parts of West Germany and Switzerland.

Prodromal symptoms of shivering, lassitude, and weakness lasted a few days and were followed by a rise in temperature up to a maximum of about 39° C. (102° F.). Headache occurred in all cases, nausea and vomiting in 73%, photophobia in 56%, and abdominal pain in 18·6%. Objective signs included meningism in 92·3%, tonsillitis in 53·1%, and enlarged cervical lymph nodes in 46·6%. Conjunctivitis occurred in 29·3% and a rash in 40%: this was polymorphic in character, mainly morbilliform, and bright red; the distribution was mostly on the trunk, seldom on face or limbs, and it lasted 2 to 8 days. Catarrhal symptoms were absent.

In 9 cases electrocardiographic abnormalities—mainly inverted T waves in Leads II and III—occurred. A relative bradycardia was present in 34·6% of all cases. In those cases with meningeal signs the cerebrospinal fluid (C.S.F.) showed a pleocytosis up to 4,480 cells per c.mm., which was maximal between the second and twelfth days of illness. The cells were mainly polymorphonuclear granulocytes at first, and later large mononuclear cells. The protein content of the C.S.F. ranged from 16 to 100 mg. per 100 ml., paper electrophoresis showing this increase to be mainly due to a rise in γ-globulin level. The mastic reaction was predominantly normal, but in 7 out of 48 cases investigated the Meinicke reaction was positive.

In 19 of 50 cases examined the electroencephalographic findings were abnormal at the height of the C.S.F. pleocytosis, this being regarded as evidence of diffuse cerebral involvement. The main finding in the peripheral blood was a leucopenia with a shift to the left. The bone marrow, when examined, was normal. The erythrocyte sedimentation rate (Westergren) varied from 4 to 40 mm. in one hour. Paper electrophoresis of the serum proteins showed a rise in the α_2-globulin fraction in the first 2 weeks of illness in 58% of the 52 cases examined.

Prognosis was uniformly good and there were no deaths. In 25 cases various sequelae (such as headache, lack of concentration, and lassitude) occurred, lasting 6 to 21 weeks. Treatment was symptomatic.

[This is a good clinical account of an outbreak similar to that which occurred at the Royal Free Hospital, London, in 1955 and to others reported from elsewhere and now regarded (as the author states in a postscript) as due to a virus of the ECHO group.]

I. M. Librach

559. **Infection with ECHO Virus Type 9.** (Erkrankungen durch Echo-Virus Typ 9)
T. BAUMANN, M. BARBEN, R. MARTI, A. HASSLER, and U. KRECH. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **87**, 307–315, March 30, 1957. 4 figs., 18 refs.

The authors describe an epidemic due to ECHO virus Type 9 which occurred in the village of Zetzwil, Aargau, Switzerland, in the summer of 1956. Of the 900 inhabitants of the village, some 150 were affected, while similar, sporadic cases occurred throughout the surrounding canton (population 400,000). Cases began to occur at the end of July and the beginning of August and fell into two groups—those without and those with meningeal signs. Males were predominantly affected, the sex ratio being 2·27 males to 1 female. The incidence among contacts was very high, an average of more than 50% of the members of each family affected, and 80% of the children and adolescents, contracting the disease.

The incubation period was 5 to 15 days. In the abortive (non-meningeal) form the temperature ranged between 38° and 40° C. (100·4° and 104° F.), falling by lysis or crisis in 1 to 5 days. The main symptoms were headache, sickness and vomiting, lassitude, anorexia, and conjunctival redness. The full form of the disease

occurred in 28 cases and was characterized by the development of meningeal signs after an initial premeningitic phase lasting usually 2 days. The average duration of the fever was 7·3 days, but those patients with meningitis were ill for 3 to 5 weeks. In the meningitic cases the cerebrospinal fluid showed a pleocytosis up to 1,643 cells per c.mm., of which 28% were mononuclear leucocytes, with a corresponding increase in protein content. The blood picture showed a tendency to leucopenia with relative lymphopenia. The average erythrocyte sedimentation rate was 13 mm. in one hour. [The technique is not specified, but the normal value is given as 2 mm. in one hour.]

In 11 of 24 cases of the meningeal form ECHO virus Type 9 was found in the faeces. [Technique of isolation not described.] In 12 cases there was a significant rise in the titre of the neutralizing antibody, the maximum value obtained being 1:64. [Again details of the technique are not given.] In 10 cases examined the stools were negative for Coxsackie virus and in 24 cases for poliomyelitis virus, while on the other hand the stools of 31 patients with poliomyelitis in the same area were negative for ECHO virus.

The authors regard ECHO virus Type 9 as a facultative neurotropic virus relatively common in serous meningitis, but only rarely leading to paralysis. The differential diagnosis in cases of infection with this virus is discussed.

I. M. Librach

560. **Benign Myalgic Encephalomyelitis**

J. F. GALPINE and C. BRADY. *Lancet* [*Lancet*] **1**, 757–758, April 13, 1957. 7 refs.

The authors report 7 cases of acute paretic illness which occurred sporadically in the Coventry area during 1956 and which resembled those observed in an outbreak of poliomyelitis-like illness among the infectious diseases staff of Whitley Hospital, Coventry, in 1953 (*Lancet*, 1954, **2**, 350; *Abstracts of World Medicine*, 1955, **17**, 71).

The clinical picture included sore throat, headache, backache, paresis of varying degree, vomiting, drowsiness, and lassitude. The accompanying fever was low in 4 cases and absent in 2, while one patient had a continued pyrexia reaching above 103° F. (39·4° C.) for 5 days. In 3 cases a swelling of the lymph nodes in the posterior cervical triangle was noted, and in one of these the blood picture was typical of infectious mononucleosis and the Paul–Bunnell reaction positive. This last patient had a history of weakness in one arm for 2 months before the acute illness and it was therefore thought unlikely that the neurological symptoms were attributable to infectious mononucleosis. Electromyographic findings were abnormal in all cases, but there was no sign of the lower motor neurone degeneration characteristic of poliomyelitis. In 3 cases electroencephalograms were recorded and were within the normal range, with minor irregularities in one case. All the patients were discharged from hospital after a stay varying from 11 days to 5 weeks. One of the 7 patients had been admitted to the hospital with a similar illness in 1953, shortly before the beginning of the outbreak among the nursing staff.

Franz Heimann

561. **Arterial Hypertension in Poliomyelitis.** [In English]

E. KEMP. *Acta medica Scandinavica* [*Acta med. scand.*] **157**, 109–118, March 25, 1957. 38 refs.

During the poliomyelitis epidemic in Copenhagen in 1952 frequent blood-pressure measurements were taken in 427 cases admitted to the Blegdams Hospital during the acute stages of the disease. Arterial hypertension [for the criteria of which the original paper should be consulted] had been found in 55% of the 100 patients who died, in 30% of the 71 survivors with encephalo-bulbar symptoms, in 45% of the 100 survivors with encephalo-bulbospinal symptoms, and in 40% of the 100 survivors with severe spinal symptoms. Hypertension was equally frequent in children and adults and in males and females. Neither artificial ventilation nor hypo- or hyperventilation seemed to be a necessary or sufficient cause for the development of the hypertension, nor did azotaemia. Histological examination of the brain in the 63 cases with hypertension amongst the 78 cases in which necropsy was performed indicated that ganglion-cell degeneration was not always present in the spinal medulla, diencephalon, and telencephalon, but was always present in the nucleus magnocellulare in the medulla oblongata. This finding is held to support the hypothesis that a prolonged rise in blood pressure in poliomyelitis treated on present-day lines is due to partial or complete destruction of the cells of the nucleus magnocellulare, which is believed to be a vasodilator centre.

A. Ackroyd

562. **Visceral Lesions in Herpes Zoster**

R. WYBURN-MASON. *British Medical Journal* [*Brit. med. J.*] **1**, 678–681, March 23, 1957. Bibliography.

The author describes 8 cases of visceral lesions in herpes zoster seen personally and summarizes a further 33 cases from the literature. The author's first case presented with a herpetic rash in the distribution of right C3 and 4 segmental areas. The visceral disturbances encountered were oedema and inflammatory changes on the right side of the larynx and trachea. In Case 2 the site of the rash was D6–8. Barium-meal examination revealed severe spasm of the pyloric antrum. In Case 3 the site of the rash was D7–8: 2 months after the onset haematemeses occurred, and later an ulcer on the lesser curvature of the stomach was demonstrated. The site of the lesion in Cases 4 and 5 was D11–L1. Both these patients had obstinate constipation and spasm of the ascending colon. In Cases 6, 7, and 8 the distribution of the herpetic eruption was between D11 and L3. Constipation, increased frequency of micturition, and dysuria were prominent clinical features; in all 3 cases a barium enema showed colonic spasm, and cystoscopy revealed inflammatory changes in the bladder mucosa.

The author concludes that in herpes zoster the segmental skin lesions may be associated with disturbances in the viscera innervated by the corresponding nerve roots. [Although it seems possible that some of the visceral disturbances described and reviewed may have had only a chance relationship to herpes zoster, this paper again illustrates the protean manifestations of the disease.]

A. G. Freeman

Tuberculosis

563. **Control of Tuberculosis. Importance of Heredity and Environment**
A. W. ANDERSON, B. BENJAMIN, R. GRENVILLE-MATHERS, and H. J. TRENCHARD. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **11**, 1–6, Jan., 1957. 1 fig., 17 refs.

An investigation into the relative importance of heredity and environment is based on the 6,537 domiciliary contacts of 2,330 cases of tuberculosis. The incidence of disease in blood-relations, spouses, and non-relatives was compared after standardization of age-specific rates. No effective hereditary factor could be found, but the degree of infectivity and the closeness of contact with the index case seemed to be related to the incidence of tuberculous disease in contacts.—[Authors' summary.]

564. **Housing and Tuberculosis in a Mass Radiography Survey**
C. Z. BRETT and B. BENJAMIN. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] 11, 7–9, Jan., 1957. 6 refs.

A possible association of housing conditions in 14,676 individual households in the Metropolitan Borough of Islington with 190 cases of active post-primary tuberculosis discovered by mass miniature radiography was investigated. The commonly found association with general economic and social circumstances was demonstrated, but there was no gradient in tuberculosis morbidity in relation to rising housing density.—[Authors' summary.]

565. **The Use of ACTH in Tuberculosis.** (Применение адренокортикотронного гормона при туберкулезе)
M. A. KLEBANOV. *Проблемы Туберкулеза* [*Probl. Tuberk.*] 28–32, No. 1, 1957. 12 refs.

The combination of ACTH (corticotrophin) with antibacterial drugs in the treatment of 30 patients with tuberculosis did not produce any exacerbation of the tuberculous process. ACTH was administered intramuscularly twice or sometimes 4 times a day, the daily dose being usually between 30 and 40 units initially and being gradually diminished so as to prevent adrenal hypofunction. The duration of the treatment varied from several weeks to several months. The most effective action of ACTH was observed in patients with acute serous effusions (pleurisy, peritonitis, pericarditis, and meningitis), the rapid disappearance of the effusions ensuring that there was very little fibrin formation and a diminished risk of adhesions. ACTH was very useful in cases of tuberculosis of bronchial lymph nodes or endobronchitis complicated by atelectasis (especially when the latter had developed recently) and also in cases of intolerance to antibacterial drugs. The use of ACTH in chronic exudative pleurisy, in amyloidosis associated with tuberculosis, and in asthmatic conditions requires to be further investigated.

The author emphasizes that ACTH must always be given in combination with antibacterial drugs, especially streptomycin. *H. W. Swann*

566. **Resistance of the Tubercle Bacillus to Drugs.** (К вопросу о лекарственной устойчивости возбудителя туберкулеза)
A. M. KHOMA-LEMISHKO. *Советская Медицина* [*Sovetsk Med.*] 48–51, No. 3, March, 1957.

Resistance of the tubercle bacillus to various antibacterial drugs may be acquired in the course of treatment or may be already present before starting treatment. This is particularly likely to occur in the chronic fibrocaseous type of disease. Out of 150 cases treated by the author, resistance to one or other of the drugs used was present in 80, and in 60 of these there was resistance to two drugs. Generally speaking, resistance increased with the length of the treatment.

The author stresses the importance of determining the resistance to drugs of the tubercle bacillus before and during treatment. *A. Orley*

RESPIRATORY TUBERCULOSIS

567. **A Study Comparing the Effects of Bed Rest and Physical Activity on Recovery from Pulmonary Tuberculosis**
J. G. HIRSCH, R. W. SCHAEDLER, C. H. PIERCE, and I. M. SMITH. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **75**, 359–409, March, 1957. 21 figs., 6 refs.

At the Rockefeller Institute Hospital, New York, the effects of alternating periods of bed rest and physical activity have been compared in the treatment of pulmonary tuberculosis in 21 adult female patients, each patient thus serving as her own control. The patients treated had far advanced or moderately far advanced recent tuberculosis and had received no previous treatment. Streptomycin sulphate, 1 g. intramuscularly 3 times a week, and isoniazid, 5 mg. per kg. body weight daily, were given over a period of 6 months in the majority of cases, PAS being substituted or added in cases where drug resistance was found. No collapse therapy or surgical measures were employed. During the bed-rest phase the patients were kept lying flat in bed except for meals and for a maximum of four brief visits to the lavatory daily, reading and listening to the radio being the only other permitted activities. The active phase was also controlled by a strict schedule, which allowed only one hour's bed rest after lunch and supper and included group exercises, occupational therapy, dancing, and games. Patients were required

to be up for 12 hours daily. Each phase was maintained for 4 weeks at a time, activity being increased gradually during the first week of each active phase.

Clinical observations included temperature, pulse, and respiration records, daily sputum measurement, and weekly weighing and physical examination. Extensive initial *x*-ray examination was followed by fortnightly plain radiography and 2-monthly tomography. Interpretation of the films was carried out by a radiologist unacquainted with the details of the study. Sputum examination was performed on 24-hour specimens every 2 weeks, with cultures on Löwenstein–Jensen medium and guinea-pig inoculation, complete sensitivity studies being carried out monthly. Blood counts, C-reactive protein tests, and estimations of the erythrocyte sedimentation rate (E.S.R.) were repeated at fortnightly intervals. The Middlebrook–Dubos haemolysin test was performed at approximately 2-monthly intervals. Patients were not discharged until 3 consecutive sputum cultures were negative for tubercle bacilli and *x*-ray appearances were stable.

Detailed summaries of all cases are presented, and it is evident from these that the course of recovery was not influenced by either bed rest or physical activity, to which adverse fluctuations in fever, sputum production, *x*-ray appearances, weight, E.S.R., and sputum culture results appeared to be unrelated. Drug-resistant bacilli appeared in only one case during treatment, though in 5 of the 21 cases drug-resistant bacilli were present before starting treatment. The over-all results were good, the sputum becoming negative on culture in all cases and all cavities being demonstrated by tomography to be closed.

The authors point out that these findings are significant only in relation to the one variable factor studied and are not applicable to the home treatment of tuberculosis. It is also noted that only relatively short-term results have been dealt with, and further studies are necessary to assess the influence of physical activity on the incidence of relapse. *B. Golberg*

568. **The Degree of Relaxation Obtained in Different Diameters of the Lung by Pneumoperitoneum and Phrenic Paralysis, when Used Either Singly or in Combination**
D. N. Shivpuri. *Diseases of the Chest* [*Dis. Chest*] **31**, 215–227, Feb., 1957. 9 refs.

569. **Corticotherapy in Chronic Pulmonary Tuberculosis Resistant to Tuberculostatic Drugs.** (La corticothérapie dans la tuberculose pulmonaire chronique résistante aux tuberculostatiques)
H. Warembourg and M. Pauchant. *Thérapie* [*Thérapie*] **12**, 22–25, 1957.

The authors report 13 cases of pulmonary tuberculosis which showed little clinical response to 3 months' treatment with streptomycin, isoniazid, and PAS, but made good progress when cortisone (75 mg. daily) was given in addition for a period of 2 months. [The title of the paper must be understood to mean that the patients' disease appeared insusceptible to antibiotic drugs and not that it was due to drug-resistant organisms. The importance of sensitivity of the tubercle bacilli to chemotherapeutic agents in determining the good effect of cortisone is mentioned in the text.] *J. Robertson Sinton*

570. **Prednisone in the Treatment of Pulmonary Tuberculosis.** (La deltacortisone dans le traitement de la tuberculose pulmonaire)
H. Brocard and M. Grivaux. *Thérapie* [*Thérapie*] **12**, 26–38, 1957. 7 refs.

The results are reported in 19 cases of pulmonary tuberculosis treated with streptomycin, isoniazid, and PAS, with the addition of prednisone in doses of 30 mg. daily for 2 months, chemotherapy being continued for some months after stopping prednisone. Cases of acute severe exudative disease showed good response. Treatment was discontinued after a week in one case because of a rising blood sugar level, while 2 patients had a slight rise in blood pressure and transient glycosuria occurred in 3 cases. With the exception mentioned above there was no change in blood chemistry or salt retention during the steroid treatment, and no evidence of suppression of adrenal activity was noted when it was discontinued. *J. Robertson Sinton*

571. **The Risk of Tuberculosis in the Corticotherapy of Malignant Blood Diseases.** (Sur les risques de tuberculose dans la corticothérapie des hémopathies malignes)
G. Marchal. *Thérapie* [*Thérapie*] **12**, 39–44, 1957.

The risk of the development of widespread tuberculosis in cases of Hodgkin's disease and acute myeloid leukaemia treated with cortisone is stressed by the author's experience of 8 cases in which this occurred. A negative tuberculin reaction may give false reassurance, and the tuberculous disease is commonly unnoticed until necropsy. Isoniazid alone appears to provide ineffective antibiotic cover, and should be given in combination with streptomycin and PAS in large doses during corticotherapy in such cases. *J. Robertson Sinton*

572. **Clinical Observations and Experimental Data on the Employment of Pyrazinamide in Tuberculous Infections.** (Osservazioni cliniche e rilievi sperimentali sull'impiego della pirazinamide nel corso della infezione tubercolare)
V. Monaldi, A. Blasi, and G. Curci. *Archivio di tisiologia* [*Arch. Tisiol.*] **12**, 3–17, Jan., 1957 [received April, 1957]. 6 figs., 10 refs.

The authors, writing from the University of Naples, describe experiments in which pyrazinamide given together with isoniazid protected guinea-pigs against challenging inoculations of tubercle bacilli far more effectively than either drug given alone.

They then describe clinical trials in which 3 g. of pyrazinamide was given with 300 mg. of isoniazid daily in cycles of 3 weeks with a week's rest in between to patients with pulmonary tuberculosis. Of the 50 patients who started treatment, 17 were withdrawn from the trial for various reasons (in 2 cases because of evidence of hepatic and in 2 of renal toxicity). In the remaining

33 cases therapy continued for between 3 and 4 months. In 9 there was no improvement, in 17 there was subjective clinical improvement only, and in 7 there was slight to moderate radiological improvement as well, cavities closing in 2 cases. All these patients had previously failed to respond to long courses of streptomycin and isoniazid. [Unfortunately no data concerning bacteriological sensitivity are provided.]

The authors postulate that pyrazinamide affects only those strains of bacteria which are resistant to isoniazid in concentrations of at least 5 to 15 μg. per ml. *in vitro*. This, they suggest, would explain its rather haphazard clinical effect and also its complementary action to isoniazid. *Arnold Pines*

573. **Cycloserine in the Treatment of Pulmonary Tuberculosis. Preliminary Clinical Results.** (La cicloserina nel trattamento della TBC polmonare. Primi risultati clinici)
B. RESCIGNO. *Archivio di tisiologia* [*Arch. Tisiol.*] **12**, 1–41, Jan., 1957 [received April, 1957]. 4 figs., 17 refs.

Writing from the University of Naples, the author describes the results of giving cycloserine to 14 patients with pulmonary tuberculosis, most of whom had previously received standard chemotherapy but still had residual lesions. They were given 1 g. of the drug daily in two doses, the total dose ranging from 30 to more than 100 g.

In 4 cases there was considerable clinical and radiological improvement, the sputum becoming negative on culture and cavities closing after subsequent operation. In 5 cases there was moderate clinical and radiological improvement, without sputum conversion, and in 5 others there was clinical improvement only. In 2 cases there was no improvement, though both these patients responded rapidly to subsequent administration of streptomycin. No resistance to cycloserine appeared, with the exception of one case in which strains resistant to 20 μg. per ml. emerged after 6 weeks. In 4 cases there were early neurotic or psychotic toxic manifestations, which apparently cleared up when administration of the drug was interrupted for a few days and the dose subsequently reduced to 0·75 g. daily. *Arnold Pines*

574. **"Open Healing" of Tuberculous Cavities**
R. F. CORPE and I. STERGUS. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] 75, 223–241, Feb., 1957. 6 figs., 16 refs.

Examination of specimens obtained at pulmonary resection in 487 cases of tuberculosis at Battey State Hospital, Rome, Georgia, revealed "open healing" of cavities in 30, the cavities being totally healed in 15 and in the healing stage in 15. The healed cavities were lined by a smooth glistening membrane, and in all cases a communicating bronchus could be demonstrated. In some instances a caseous focus was found nearby. The healing cavities showed occasional foci of granulation tissue and, rarely, tiny tubercles in the wall. Open healing was observed three times more frequently in negroes than in white patients; it was not seen in white females. It occurred most frequently after treatment with a combination of streptomycin, isoniazid, and PAS. The sputum of patients with open healing of cavities had been free from tubercle bacilli for an average of 15 months before resection. Only 2 cavities yielded tubercle bacilli on culture.

In the authors' view this pathological picture has been seen with increasing frequency since the introduction of isoniazid. They recommend removal of the cavity if the patient is fit in view of the possibility of complications, and for patients with a negative sputum but residual cavitation following drug therapy in whom surgery is contraindicated, careful supervision with continued chemotherapy. *Denis Abelson*

575. **The Syndrome of Persistent Cavitation and Non-infectious Sputum during Chemotherapy and Its Relation to the Open Healing of Cavities**
O. AUERBACH and M. J. SMALL. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] 75, 242–258, Feb., 1957. 8 figs., 35 refs.

The syndrome of persistent cavitation with a negative sputum has become a frequent finding since the introduction of prolonged chemotherapy and the greater use of isoniazid. Of 31 such cases in which the lesion had been resected at the Veterans Administration Hospital, East Orange, New Jersey, the authors found that in only 11 was there true "open healing" as determined by histological examination—that is, with no necrotic foci in the walls, no necrotic cavitary contents, and no necrotic lining. The radiological demonstration of a thin-walled, cyst-like cavity was a likely, but not absolute, indication of open healing. On the other hand the length of time during which the sputum had been negative could not be related to the incidence of cavitary healing. For example, in one case the cavity was found to be healed only 2 months after the last positive sputum, whereas in another pathological evidence of active disease was present although the sputum had been negative for 60 months.

The authors conclude that prolonged chemotherapy, by the prevention of further necrosis of cavity walls and by the promotion of epithelization at the junction of the cavity with the bronchus, encourages emptying of the cavity and promotes its healing, but that it is not yet possible to forecast from clinical and radiological evidence whether true open healing will be found on pathological examination of the resected lesion.
A. M. Macarthur

576. **Bilateral Resection in the Treatment of Pulmonary Tuberculosis**
F. H. COLE, E. P. BOWERMAN, and L. C. PRIETO. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] 75, 259–265, Feb., 1957.

Resection was carried out in 900 cases of pulmonary tuberculosis at the West Tennessee Tuberculosis Hospital, Memphis, between 1949 and 1955, but a bilateral operation was recommended in only 60, and actually performed in 33. Operation on the second side was considered unnecessary in 13 of the remaining 27 and inadvisable in 9. Most of the patients subjected to

bilateral resection were under 40 years of age, and 22 of them lost at least one lobe. Residual nodular lesions, open cavity, and bronchial destruction were the commonest indications for the second operation, which was carried out 10 to 24 weeks after the first. Although sputum cultures were mostly negative at the time of operation, tubercle bacilli were found in 43 of 66 resected specimens. In 4 cases sputum was positive after bilateral resection. There were 2 deaths—one after unilateral and one after bilateral resection. The age of the patient, duration of the disease, and the occurrence of post-operative complications had a marked influence on the outcome. *Denis Abelson*

577. **The Results of Pulmonary Resection in the Treatment of Tuberculosis: An Evaluation of 201 Consecutive Resections**
J. C. COOLEY, F. H. MOSER, and G. A. HEDBERG. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **33**, 383–389, March, 1957. 5 refs.

The authors have analysed the results of 201 pulmonary resections performed between 1951 and 1955 on 189 patients with pulmonary tuberculosis. All the patients in the series received chemotherapy, usually both before and after operation and in most cases for a total period of 6 to 18 or more months. The most frequent operation was segmental resection, only 13 cases of pneumonectomy being included in the series. The operative mortality was 4·2%. The results in the survivors were largely assessed from the culture of gastric lavage specimens and were classified as " good " in 85%. Bilateral resection was carried out in 12 cases, of which 3 were classed as failures. *J. R. Belcher*

578. **Simultaneous Bilateral Resection with a Space-diminishing Procedure for Pulmonary Tuberculosis**
V. O. BJÖRK. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **33**, 617–624, May, 1957. 6 figs., 8 refs.

EXTRA-RESPIRATORY TUBERCULOSIS

579. **Corticotropin and Adrenal Steroids as Adjuncts to the Treatment of Tuberculous Meningitis**
J. R. JOHNSON, N. E. FURSTENBERG, R. PATTERSON, H. K. SCHOCH, and W. N. DAVEY. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 316–331, Feb., 1957. 8 figs., 11 refs.

At the Veterans Administration Hospital, Ann Arbor, Michigan, 5 selected patients aged 30 to 71 years were treated for severe tuberculous meningitis with a prolonged continuous course of isoniazid, streptomycin, and PAS (without intrathecal treatment). In addition they were given intermittent courses of systemic corticotrophin or cortisone in full doses, the duration of the courses varying between 7 weeks and 4 months. In 4 cases striking improvement was noted during steroid therapy, but relapse followed its discontinuation or a reduction in dosage in 3 cases. Resumption of steroid therapy in full doses again produced a good clinical response in these cases, and subsequent gradual withdrawal of the drugs, usually covered by the administration of corticotrophin, did not result in a further relapse. One old lady of 71 was in coma on admission and remained unconscious until her death 3 months later. At necropsy oedema of the cerebral hemispheres and scattered petechial haemorrhages in the white matter were found. Large areas of ischaemic necrosis of the cerebrum were present, but there were no lesions or exudate of any sort which could be identified as the residua of the meningitis.

[The only evidence of meningitis in one case was a raised cerebrospinal-fluid protein level in a patient with paraspinal tuberculous abscess. The cell count was normal and no tubercle bacilli were demonstrated. This was not a case of meningitis. In 3 other patients with bacteriologically proven meningitis the symptomatic improvement during steroid therapy was impressive.] *John Lorber*

580. **Adrenocortical Capacity in the Acute Stage of Tuberculous Meningitis.** [In English]
M. OKA, K. ÖSTERLUND, M. PAATELA, and O. WASZ-HÖCKERT. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **24**, 402–406, April, 1957. 1 fig., 7 refs.

Cortisone or hydrocortisone has been used as a routine adjuvant to antibiotics in the treatment of tuberculous meningitis at the University Children's Clinic, Helsinki, since 1954, sometimes with striking and even life-saving effect. In this paper the authors describe a study of adrenal function in 5 children aged 6 to 14 years with tuberculous meningitis to whom 10 mg. of ACTH (corticotrophin) was given by intravenous infusion within a few days of admission and 8 to 30 days from the onset of the symptoms of meningitis, the subsequent changes in plasma 17-hydroxycorticosteroid level and in the eosinophil count being used as a measure of adrenal capacity. Similar investigations were performed on 8 healthy children who acted as controls. Both the initial level of 17-hydroxycorticosteroids in the plasma (mean, 26 μg. per 100 ml.) and its maximum elevation during the infusion of ACTH (mean, 78·6 μg. per 100 ml.) were much higher in the patients with meningitis than in the controls (means, 17 μg. per 100 ml. and 41·8 μg. per 100 ml. respectively). Before and after the infusion the mean eosinophil counts were 58·6 and 2·4 per c.mm. respectively in the cases of meningitis and 379 and 26·6 per c.mm. respectively in the controls.

It is concluded that in the early stage of tuberculous meningitis the adrenal cortical response to ACTH is increased and that the beneficial effect of steroid adjuvant therapy in such cases cannot be due to an insufficiency of endogenous hydrocortisone, but must be attributed to " some defect in the mechanism involved in the use of this hormone ".

Full details of the techniques used are provided. *John Lorber*

581. **The Treatment of Endometrial Tuberculosis with Streptomycin and PAS. A Report to a Joint Subcommittee of the British Tuberculosis Association and the Royal College of Obstetricians and Gynaecologists**
A. M. SUTHERLAND. *Tubercle* [*Tubercle* (*Lond.*)] **38**, 46–51, Feb., 1957. 3 refs.

Venereal Diseases

SYPHILIS

582. **Further Assessment of Cardiolipin Antigen by Parallel Testing against Standard Antigen in Routine Wassermann Reactions**

S. SHAW. *British Journal of Venereal Diseases* [*Brit. J. Vener. Dis.*] 33, 22–24, March, 1957. 5 refs.

Between February, 1955, and February, 1956, the Wassermann reaction was carried out at the Charing Cross Hospital, London, on 3,588 routine specimens of serum with cardiolipin antigen and standard antigen in parallel tests. Comparison of the results from 1,373 of these sera (excluding antenatal specimens) showed agreement in 95·1% and disagreement in 4·9%, cardiolipin antigen giving some result while the standard antigen gave a negative or doubtful result in 4·8% and the standard antigen giving a greater reaction than cardiolipin antigen in only 0·1%. With 92 sera from syphilitics, included in the above, there was agreement between the results in 44 cases and disagreement, with cardiolipin antigen giving a greater reaction than standard antigen, in 48.

Cardiolipin was thus demonstrated to be the more sensitive antigen with syphilitic sera. On the other hand cardiolipin antigen gave 1·6% of non-specific reactions and standard antigen only 0·5%. Similarly, in the examination of 2,215 antenatal sera cardiolipin antigen gave 4% of non-specific reactions and standard antigen only 0·3%. *R. R. Willcox*

583. **Quantitative Studies of Lipid-soluble Tissue Antigens as Exemplified by the Wassermann Antigen–Antibody System. I. Estimation of the Wassermann Antibody in Absolute Weight Units**

A. G. OSLER and E. A. KNIPP. *Journal of Immunology* [*J. Immunol.*] 78, 19–29, Jan., 1957. 2 figs., 23 refs.

In this paper from the Johns Hopkins Hospital and School of Hygiene and Public Health, Baltimore, a procedure is described for the quantitative estimation of the Wassermann antibody. The antibody-containing aggregates resulting from the interaction of syphilitic serum with an antigen containing cardiolipin, lecithin, and cholesterol are washed and heated with 6N hydrochloric acid under pressure. Ninhydrin is added and the *p*H adjusted to 5·0 with 6N sodium hydroxide. A blue colour is produced by the reaction of ninhydrin with the α-amino groups set free by the acid hydrolysis and its intensity is measured spectrophotometrically. Commercial preparations of human γ globulin are used as reference proteins to enable the ninhydrin colour values to be related to γ-globulin nitrogen concentrations. [Reference should be made to the original paper for details of the technique, which is said to be capable of detecting as little as 10 μg. of antibody nitrogen with an approximate error of 1 μg.]

The antigen used was a saline suspension containing cardiolipin, lecithin, and cholesterol in the weight ratios 1 : 8 : 20. Interaction of serum and antigen for 6 days in a refrigerator was necessary to obtain the maximum precipitation of antibody. Antigens containing cardiolipin alone failed to remove all the antibody from the serum. No antibody could be demonstrated in sera on which the V.D.R.L. test had given a negative result. Normal serum, either fresh or after heating to 56° C. for 30 minutes, diminished the formation of specific aggregates with syphilitic serum and had a solvent action when added to precipitates which had already been formed. In contrast, the addition of normal rabbit serum to a syphilitic rabbit serum increased the amount of precipitable nitrogen, possibly owing to binding of complement. Inactivation of complement by the customary heating to 56° C. for 30 minutes showed that about 83% of the Wassermann antibody in a syphilitic rabbit serum was lost by this treatment; in human serum the loss was about 30%. Removal of complement from syphilitic rabbit sera by the addition of the washed precipitate from an anti-bovine-albumin serum with its homologous antigen or by the addition of a chelating agent also diminished the amount of precipitable nitrogen compared with the values obtained with untreated serum. Removal of complement in these experiments was not complete, as the serum still had some haemolytic activity.

Determinations of the maximum precipitable nitrogen in syphilitic sera showed good agreement with the values calculated from the Heidelberger–Kendall equation. They also showed that as little as 0·014 μg. of Wassermann antibody nitrogen may be detected by the V.D.R.L. test. *A. E. Wilkinson*

584. **Quantitative Studies of Lipid-soluble Tissue Antigens as Exemplified by the Wassermann Antigen–Antibody System. II. Comparative Studies with Mammalian and Plant Tissue Phospholipids**

A. G. OSLER and E. A. KNIPP. *Journal of Immunology* [*J. Immunol.*] 78, 30–44, Jan., 1957. 6 figs., 28 refs.

Using the technique for estimating Wassermann antibody nitrogen described in the previous paper [see Abstract 583], the authors have shown that antigens containing cardiolipin prepared from either human or beef heart muscle are equally effective in precipitating the antibody from syphilitic human or rabbit serum, or from the serum of rabbits artificially immunized with cardiolipin antigens. Sitolipin, a phosphatide obtained from wheat germ, and cardiolipin extracted from human liver were found to be less effective than the preparations from human or bovine heart muscle.

Quantitative complement-fixation tests also showed that antigens made with cardiolipin from human or beef heart muscle produced equal degrees of fixation with human syphilitic serum or with the serum of rabbits

immunized with either phospholipid. In contrast to the findings in flocculation tests, antigens containing cardiolipin from human liver tissue gave greater degrees of fixation than those in which the phospholipid was prepared from heart tissue. When the components of the cardiolipin–lecithin–cholesterol antigens were examined separately it was shown that human or beef heart cardiolipin can fix only minimal amounts of complement with Wassermann antibody unless lecithin is present as well. This held good whether cholesterol was present in the antigen or not. Wassermann antibody would, however, fix some complement when lecithin alone was used as antigen; this was found to be the case not only with the natural product from beef heart, which might have contained traces of cardiolipin as impurity, but also to a lesser degree with synthetic L-α-(dimyristoyl) and L-α-(dioleyl) lecithins.

The Wassermann antibody and that found in sera giving non-specific reactions in serological tests for syphilis appear to react similarly with cardiolipins produced from various sources. This suggests that in some individuals the Wassermann antibody may represent a response to an antigenic tissue component. In treponemal infections the antibody may have a dual origin, coming both from an antigenic fraction of the treponeme as yet unidentified and from the tissue antigen.

A. E. Wilkinson

585. **The Iodine Test in the Detection of Biological False Positive Tests for Syphilis.** (Il test allo jodio, quale orientamento nelle reazioni aspecifiche per la lue)
M. TORCHI. *Archivio italiano di dermatologia sifilografia e venereologia* [*Arch. ital. Derm.*] **28**, 265–285, 1956 [received April, 1957]. 21 refs.

The author points out that while true positive reactions in the serological tests for syphilis are due to the presence of specific antibody globulin, globulins which react similarly with the antigens used, but which are not necessarily identical, may occur in the blood in numerous conditions in which protein metabolism is altered. Although such conditions are usually associated with an increase in the globulin and a decrease in the albumin fraction of the plasma proteins, the demonstration of these changes is of no help in distinguishing biological false positive from true positive reactions. For this purpose he suggests the use of a simple iodine test described by Mallén in 1950. [No reference is given.] This consists in mixing on a glass slide one drop of Lugol's iodine solution with a drop of clear serum. The result is read in 1 to 2 minutes under the low power of the microscope, a positive reaction being indicated by a blackish precipitate and graded quantitatively from + to ++++. In a negative reaction the serum remains quite clear.

This test is found to give consistently negative results in healthy individuals, and the result is also negative in syphilitics, regardless of their serological findings, except in recent primary and secondary cases, in which it is positive. Thus of 139 iodine tests carried out on syphilitic sera at the Civil Hospital, Bolzano, 127 (91%) gave a negative result. Of the remaining 12 patients, 7 were suffering from conditions involving a plasma protein upset and the remaining 5 had either a chancre or syphilitic roseola. It is suggested that in early cases of syphilis such as these 5 an antibody globulin which has not yet become differentiated to the mature, non-iodine-reacting type is probably present.

The iodine test was also carried out on sera from 286 medical patients in parallel with 3 complement-fixation tests with different antigens and 2 flocculation reactions, the Meinicke (M.K.R.II) and citochol reactions. In 89% all the tests gave negative reactions. In 8% there was a positive iodine reaction together with a biological false positive reaction with one or more of the serological tests; these patients were suffering from various diseases including bronchopneumonia, hepatitis, rheumatism, polyarteritis, and cachexia, and it is claimed that the positive iodine reaction helped to reveal their positive serological reactions as biologically false. Negative serological reactions associated with a positive iodine reaction were found in 10 cases (3%), this result being interpreted as due to a mild dysproteinaemia, as yet insufficient to produce a false positive serological reaction. In a single case a false positive serological reaction was associated with a negative iodine reaction, providing an important reminder that the iodine test is not infallible. Detailed analysis of the results of the serological tests in the above series and their correlation with those of the iodine test and with the plasma protein pattern show that a positive iodine reaction is more often associated with non-specific flocculation reactions than with non-specific complement-fixation reactions.

F. Hillman

586. **Proposed Methods of Increasing the Sensitivity of the Nelson–Mayer T.P.I. Test and Their Practical Application.** (Vorschläge zur Methodik eines T.P.I.-Testes Nelson Mayer mit grösserer Empfindlichkeit und deren praktische Anwendung)
G. EHRMANN. *Archiv für klinische und experimentelle Dermatologie* [*Arch. klin. exp. Derm.*] **204**, 37–51, 1957. 12 refs.

The technique of performance of the treponemal immobilization (T.P.I.) test has been studied in detail by the author at the University Clinic for Venereal and Skin Diseases, Vienna, with a view to increasing its sensitivity. Increasing the reaction time beyond 18 hours was found to increase the sensitivity of the test by only a very small amount. The optimum temperature is considered to be 35° to 36° C., a higher temperature producing a more rapid reaction but giving an increased number of inconclusive results. The stability and activity of complement are regarded by the author as the most important single factors. Increasing the amount of residual complement did not make the test more sensitive. However, an increase in sensitivity was considered to occur when the tubes were shaken after 12 hours and the incubation period prolonged up to 25 hours, this conclusion being reached after the examination of 381 specimens of serum. In 23 cases the result was negative when the test was performed by the usual methods, but became positive when the tubes were shaken after 12

hours, while 16 sera which gave negative or doubtful results by the usual technique gave either doubtful or positive results when this modification was introduced.

R. D. Catterall

587. **Complement Titration and a Complement-fixation Reaction with *Treponema pallidum*.** (Eine Komplement-Titer- und Komplement-Bindungsreaktion mit *Treponemata pallida*)

K. MEINICKE. *Hautarzt* [*Hautarzt*] 7, 540–543, Dec., 1956. 4 refs.

In this paper from the University of Munich the author describes a series of tests in which he estimated the titre of complement present both before and after carrying out the treponemal immobilization (T.P.I.) test. [For details of the techniques used the original paper should be consulted.] With sera that were positive to the standard serological tests (S.T.S.) there was a fall in the complement titre of 8 to 10 units, whereas with sera negative to the S.T.S. the fall in complement titre was only 2 to 4 units. The results of the complement titration and the T.P.I. tests were in agreement in most instances.

A complement-fixation test is also described, the antigen for which was prepared from a virulent strain of *Treponema pallidum* extracted from rabbits' testes not more than 8 days after inoculation. The suspension was washed, centrifuged, and passed through a filter. The washed treponemes were then resuspended in 0·3% phenol saline and the concentration standardized at 20 to 30 treponemes per microscope field. Other reagents used in the reaction were inactivated serum, complement, and a haemolytic system. [Details of the technique should again be studied in the original paper.]

The results given by this test were compared with those of the T.P.I. test and S.T.S. in 20 cases. There was a considerable measure of agreement in the case of the T.P.I. test, but agreement was not so marked in the case of the S.T.S., and the author discusses reasons for this difference.

[This work will be of considerable interest to serologists at the present time in view of the description below by Price and Whelan of the treponemal Wassermann reaction (see Abstract 588).] *R. D. Catterall*

588. **Preliminary Report on a Complement-fixation Test for Treponematosis (TWR)**

I. N. O. PRICE and M. J. WHELAN. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] 33, 18–21, March, 1957. 7 refs.

The preparation from virulent *Treponema pallidum* of an antigen for use in the serological diagnosis of syphilis is reported from the London Hospital and its use in a complement-fixation reaction—the treponemal Wassermann reaction (T.W.R.)—is described. [For technical details of the preparation of the antigen the original paper should be consulted.]

When 1,030 sera were tested by this method in parallel with the standard Wasserman reaction (W.R.) there was agreement between the results in 946 cases (92%) and disagreement in 84 (8%). Of the latter group, 10 gave a positive W.R. and a negative T.W.R., 7 of these sera being from syphilitic patients, one from a coloured person from an area in which yaws is endemic, one from a non-treponemal reactor, and one was non-classifiable. A positive T.W.R. and a negative W.R. were given by 74 sera. Of these, 25 were from persons suffering from syphilis, 8 from patients suffering from yaws, 33 from coloured patients from areas where yaws is endemic, 2 from non-treponemal reactors, and 6 were non-classifiable. All of these sera came from a venereal diseases clinic. A further 1,205 sera from a general hospital were tested by both methods. The results from 1,171 (97%) were in agreement and from 34 (3%) were discordant. Out of 1,044 " problem sera " which had previously given anomalous reactions, the results of the two tests were in agreement in 886 cases (85%) and discordant in 158 (15%).

A total of 785 of these problem sera were examined in parallel by the T.W.R. and the treponemal immobilization (T.P.I.) test. One or other or both tests gave invalid results with 50 of these, and of the remaining 735, the results in 670 cases (91%) were in agreement, while those in 65 (9%) disagreed. Of the latter sera, 30 were from patients suffering from syphilis, one from a patient suffering from yaws, 11 from coloured patients from areas in which yaws is endemic, 19 from non-treponemal reactors, and 4 were non-classifiable. It is concluded that " neither test has any significant advantage over the other as far as sensitivity or specificity is concerned ", and that " the TWR demonstrates serum reactors much more frequently than the TPI when sera from coloured patients are tested ".

The authors consider that the preparation of the antigen should be " well within the competence of any reasonably equipped laboratory ". The antigen is stable and the amount obtained per rabbit (enough for 900 to 1,400 tests) is economic. The results obtained in this preliminary trial " give rise to a strong hope that this specific test will soon be a practical procedure for the *routine* serological diagnosis or exclusion of treponemal infections ".

[This hope will be echoed by all venereologists who have not enjoyed the advantage of adequate facilities for performance of the T.P.I. test. The new test may well render the more complicated immobilization test out of date.] *R. R. Willcox*

589. **Comparison of Results given by a Complement-fixation Test for Syphilis using the Reiter Treponeme as Antigen with the Treponemal Immobilization Test**

A. E. WILKINSON. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] 33, 25–29, March, 1957. 19 refs.

At the Venereal Diseases Reference Laboratory (M.R.C.), London Hospital, a series of parallel tests were carried out on 1,085 sera, the tests used being the Wassermann reaction with a crude heart-extract antigen, the Kahn test, the Price precipitation reaction, a complement-fixation test using a suspension of the Reiter treponeme as antigen, and the treponemal immobilization (T.P.I.) test. The sera included 196 from syphilitic patients, 342 which had given positive reactions on

routine testing, 216 from patients with suspected latent syphilis, 218 which had given negative or equivocal results with routine tests but came from patients who had lesions or histories suggestive of syphilis, and 36 from patients with conditions often associated with false positive serum reactions for syphilis.

The Reiter complement-fixation test was found to be more sensitive than the conventional tests in cases of untreated early syphilis and in latent and late symptomatic syphilis. With " problem sera " the Reiter complement-fixation test gave results which were in closer agreement with those of the T.P.I. test than with those of conventional serum tests. Its specificity was also higher than that of the conventional tests as judged by comparison with the results of the T.P.I. test.

R. R. Willcox

590. **Benzathine Penicillin G in the Treatment of Syphilis**
C. A. SMITH, M. KAMP, S. OLANSKY, and E. V. PRICE. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **15**, 1087–1096, 1956 [received March, 1957]. 4 figs., 5 refs.

The results obtained with benzathine benzylpenicillin in the treatment of syphilis, and preliminary experience with this drug in asymptomatic neurosyphilis, are reported. A single injection of 2·5 mega units of benzathine benzylpenicillin, which in most instances produces and maintains a detectable blood level for periods up to 3 weeks, was given in all cases. There were no failures in 52 cases of primary seronegative syphilis, but of 67 patients with seropositive primary syphilis, 2 required further treatment—one for serological relapse and one for re-infection. In a series of 155 cases of secondary syphilis the cumulative re-treatment rate was 5·5%, re-infection being the cause in 4·6%. These results were better than those achieved with 4·8 mega units of penicillin with aluminium monostearate (P.A.M.) administered at a single session or at 2, 3, or 4 sessions. The seronegativity rates 2 years after treatment were: primary seronegative syphilis 100%, seropositive primary disease 96%, and secondary syphilis 94·5%.

The authors compare the results in 47 cases of asymptomatic neurosyphilis treated with one dose of 2·5 mega units of benzathine benzylpenicillin with those obtained in 53 such cases given P.A.M. in a dose of 4·0 to 5·9 mega units. In all cases the cerebrospinal-fluid findings were abnormal, with pleocytosis (over 20 per c.mm.), increased protein content, and a positive response to the complement-fixation test for syphilis. Although the series was not large, it is significant that 18 months after treatment 21% of the group given benzathine benzylpenicillin had relapsed compared with 10·5% of the group treated with other penicillin preparations; 25 months after treatment the relapse rate in the latter group had risen to 15·8%. The authors consider these preliminary data to show that one dose of 2·5 mega units of benzathine benzylpenicillin is not enough for asymptomatic neurosyphilis. The schedule of dosage with other penicillin preparations (4·0 to 5·9 mega units) was also unsatisfactory.

Reactions to treatment were not troublesome. Altogether some 7,000 cases have been treated with benzathine benzylpenicillin, and the incidence of reactions has remained about the same—2·39 per 1,000. This compares favourably with an incidence of 4·52 per 1,000 patients treated with P.A.M. Urticaria was the most common side-effect. There was no tendency to delayed reactions as a result of long-sustained levels of penicillin in the blood.

Robert Lees

591. **Comparative Study of Two Types of Treatment in 250 Cases of Early Syphilis.** (Estudio comparativo de dos tipos de tratamiento en 250 casos de lues reciente)
P. B. LÓPEZ. *Boletín de la Sociedad cubana de dermatología y sifilografía* [*Bol. Soc. cubana Derm. Sif.*] **13**, 111–117, Sept., 1956 [received March, 1957].

The author presents the results of treatment, at the Dr. Carlos J. Finlay Military Hospital, Cuba, of 235 cases of primary and secondary syphilis, of which 144 received crystalline benzylpenicillin by intramuscular injection in addition to arsenoxide and bismuth, while 91 received penicillin and bismuth only. The comprehensive follow-up schedule adopted is outlined. On the completion of 6 to 8 months of post-treatment observation the patients were readmitted to hospital for detailed study, including examination of the cerebrospinal fluid. Since the cure rate at that time was 97% in both groups the author concludes that arsenic should no longer be used in the treatment of syphilis.

[It would seem from the figures given for the incidence of seroresistance, serorelapse, and neurosyphilis and the development of open lesions in the two groups that the ultimate cure rate was below the figure of 97%, but the duration of follow-up to which these figures relate is not stated.]

Eric Dunlop

GONORRHOEA

592. **Failure of Silver Nitrate Prophylaxis for Gonococca Ophthalmia Neonatorum**
H. E. PEARSON. *American Journal of Obstetrics and Gynecology* [*Amer. J. Obstet. Gynec.*] **73**, 805–807, April, 1957. 10 refs.

From a review of the literature and his own experience the author suggests four possible reasons for the failure of silver nitrate prophylaxis to prevent the occurrence of gonococcal ophthalmia neonatorum: (1) the drug is of little or no value; (2) it is not properly administered; (3) infection occurs from adjacent skin after the drug has been dissipated; and (4) failure on occasion to implement routine use of the drug. During the 10 years 1946–56 there were 67,200 live births at the Los Angeles County Hospital. All the babies were treated as a routine before leaving the delivery room with 1% silver nitrate eye-drops, the eyelids being held apart by a nurse and the drops inserted by a resident, intern, or medical student. Despite this there were 40 instances of gonococcal ophthalmia neonatorum. Nearly half the babies involved were prematurely born. In more than half of the cases the diagnosis of gonococcal ophthalmia was made on the 3rd or 4th day of life. Two infants had gonococcal ophthalmia at birth; in these two cases the

membranes had been ruptured for 24 and 48 hours respectively before delivery.

Commenting on his findings, the author states his opinion that liability to infection is probably conditioned by the number of gonococci present in the maternal cervix at the time of delivery. The greater risk to prematurely born infants which is apparent is presumed to be due to the poorer resistance to infection of the immature foetus. *R. S. Morton*

593. **Benzathine Penicillin G in the Control of Gonorrhoea**
C. E. Hookings and L. M. Graves. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **33**, 40–42, March, 1957. 3 figs., 4 refs.

The inadequacy of the treatment of gonococcal infection in female patients with a single dose of 600,000 units of benzylpenicillin plus 2% aluminium monostearate (P.A.M.) was shown by the recognition of 15% of these women as contacts of infected men within 60 days of that treatment. Measures designed to bring contacts of infected males for examination and treatment within 72 hours of being named proved remarkably successful, but did not reduce the incidence of gonorrhoea in men in the area. The treatment was then changed to 600,000 units of P.A.M. plus 1·2 mega units of benzathine benzylpenicillin, which is reputed to have an antigonococcal action for 16 days. Following such treatment the proportion of women renamed as infecting contacts within 60 days fell to 1·7% and there was a decline in the attendance of male patients. Subsequently the combined therapy was given to male patients, since when there has been a further decline in the attendance of men.

From their findings the authors conclude that the combined treatment is the method of choice, while speedy investigation and treatment of female contacts are also of importance. *V. E. Lloyd*

594. **Oral Potassium Penicillin G Combined with Probenecid in the Treatment of Gonorrhea in the Male**
M. Marmell and A. Prigot. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 256–258, March, 1957. 3 refs.

An investigation was undertaken at Harlem Hospital, New York, to determine the optimum dose and dosage schedule for a combination of oral penicillin and probenecid in the treatment of gonorrhoea in the male, this combination having been reported to give higher blood levels of penicillin and to maintain them over a longer period of time than penicillin administered alone. All the patients studied presented clinical and laboratory evidence of gonorrhoea before treatment, and were considered cured if smears and cultures became negative for a minimum of 6 days after treatment. The drugs were given in the form of tablets, each containing 100,000 units of crystalline potassium benzylpenicillin and 0·25 g. of probenecid. Of the 6 dosage schedules employed, 3 provided 800,000, 600,000, and 400,000 units of penicillin respectively combined with 0·25 g. of probenecid per 100,000 units given in divided doses over 24 hours, two provided single doses of 300,000 and 400,000 units of penicillin respectively combined with probenecid in the same proportion, and one provided a single dose of 400,000 units of penicillin plus 1·5 g. of probenecid. Of 129 patients treated, 92 were adequately followed up.

All of 22 patients treated with 800,000 units or 600,000 units of penicillin in combination with 0·25 g. of probenecid per 100,000 units in divided doses were cured, as were all but one of 13 receiving 400,000 units of penicillin plus 0·25 g. of probenecid per 100,000 units in divided doses (92% cure). A single dose of 400,000 units of penicillin with probenecid in the same proportion resulted in 3 failures out of 27 patients treated (88% cure), and increasing the amount of probenecid given with the same dose did not improve the cure rate (8 out of 10 patients). Only 5 of 8 patients treated with a single dose of 300,000 units of penicillin and 0·75 g. of probenecid were cured. There were no toxic reactions from the drugs.

The authors conclude that oral benzylpenicillin given effectively can cure gonorrhoea in the male when the dosages approach those used in parenteral therapy, but that single-dose schedules are less satisfactory.

[It is debatable whether, in gonorrhoea, oral administration presents any advantage over parenteral administration of penicillin. The study would have been of much more value if the numbers in each group had been greater and if a contol series had been treated without probenecid.] *Leslie Watt*

595. **Gonococcal Infection in Teen-aged Girls and Mature Women**
L. Z. Goldstein. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **33**, 34–39, March, 1957. 3 figs., 8 refs.

During the years 1951–3, 383 adult women and 155 teen-age girls suspected of having gonorrhoea were referred to the Albert Einstein Medical Center, Philadelphia. All the women and the majority of the teenagers were sexual contacts of men treated for acute urethritis. As a public-health measure all cases were treated with 1·2 mega units of aqueous penicillin; all those in whom laboratory tests (film and culture) showed gonococcal infection were re-examined a week later. Positive results of tests were obtained in 30 (19·3%) of the teen-agers and 81 (21·1%) of the adults. The pelvic lesions found on clinical examination are listed in a detailed table. The gonococcus was isolated in 13 cases in which the cervix appeared healthy. Although stained films revealed the gonococcus in 66 contacts, the author considers the cultural method to be more useful, but stresses that its value is proportional to the efficiency of the media and the technical and diagnostic skill of the bacteriologist. *V. E. Lloyd*

596. **An Outbreak of Gonorrhea and Early Syphilis in Massachusetts**
N. J. Fiumara, J. D. Shinberg, E. M. Byrne, and J. Fountaine. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 982–990, May 23, 1957. 1 fig., 7 refs.

Tropical Medicine

597. **The Use of *iso*Propylsulphones in Leprosy. I. Mode of Action. II. Therapeutic Results.** (Emploi de sulfones isopropylées dans la lèpre. I. Mode d'action. II. Résultats thérapeutiques)
H. FLOCH and F. DEHEZ. *Bulletin de la Société de pathologie exotique et de ses filiales* [*Bull. Soc. Path. exot.*] **49**, 1089–1092 and 1093–1097, Nov.–Dec., 1956 [received April, 1957]. 1 ref.

At the Hôpital Plui Doan and Institut Pasteur, Hanoi, Viet-Nam, the authors have treated a small series of cases of leprosy with two *iso*propylsulphones. Both compounds are derivatives of dapsone, being respectively di-(4:4′-*iso*propylaminophenyl) sulphone (3460 C.T.) and 4-amino-4-*iso*propylaminodiphenyl sulphone (3461 C.T.), and are administered orally. In man the mono-substituted compound dissociates freely and a dosage of 200 mg. daily gives a blood level of sulphone equivalent to that obtained with 170 mg. of dapsone. The di-substituted compound is more stable, and 200 mg. daily is the equivalent of only 50 mg. of dapsone.

The latter drug has been used in 3 cases of leprosy so far—2 of tuberculoid and one of mixed type, the dosage being 200 mg. daily for 6 days a week. The 2 tuberculoid cases have improved clinically, but it is too early yet to judge the effect in the mixed case. The mono-*iso*propyl compound has been given in 8 cases in the same dosage. In 3 lepromatous cases the duration of treatment has been too short as yet for assessment. One patient who had been subject to repeated reactions suffered a further reaction and treatment was stopped. The remaining 4 cases—2 lepromatous, 1 mixed, and 1 tuberculoid—appear to be doing well; the mixed case has become bacteriologically negative after 7 months of treatment. The drugs are well tolerated, only one case of reaction occurring so far. *William Hughes*

598. **An Analysis of the Results of the Treatment of Yaws with a Single Injection of Procaine Penicillin with 2% Aluminium Monostearate**
J. C. HUME and G. FACIO. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **15**, 1057–1085, 1956.

In Haiti a total of 1,049 patients with yaws were treated with a single injection of procaine penicillin with aluminium monostearate (P.A.M.). The criteria for inclusion in the group studied were the presence of dark-field positive lesions and a positive reaction to serological tests, including quantitative and qualitative flocculation tests using the V.D.R.L. technique with cardiolipin antigen and the Kahn technique with standard antigen. An intramuscular injection of 150,000, 300,000, or 600,000 units of P.A.M. was given, the majority of patients (826) receiving 600,000 units. Of this group of 826 patients, 74·5% were followed up for 2 years after treatment, and analysis of the results showed that the cumulative re-treatment rate was very gratifying. The authors emphasize, however, that these results cannot be compared with those obtained with P.A.M. in syphilis. Approximately 30% of the patients were seronegative after 2 years, a finding in line with previous experience of the serological response to adequate therapy in yaws. Neither sex nor age appeared to have any influence on the results. The criterion for re-treatment was the re-appearance of dark-field positive lesions, some of which were considered to be due to re-infection rather than to relapse.

The results obtained with 300,000 units of P.A.M. were surprisingly good, and although the series was too small for statistical comparison with the group given 600,000 units, the impression was that the results were much the same, with a slightly higher rate of reversal of positive serological reactions in the lower-dosage group. It is concluded that a single dose of 600,000 units of a reliable preparation of P.A.M. which conforms to the standards laid down by W.H.O. is the method of choice for mass treatment campaigns against yaws, where control of infectiousness is the primary aim. The criteria for re-treatment should probably be based on a confirmed rise in serological titre one month or more after treatment or maintenance of the original titre for 6 months after treatment. *Robert Lees*

599. **Value of Rectal Biopsies in the Diagnosis and Treatment of *Schistosoma mansoni* Infections**
L. C. SPINGARN, M. H. EDELMAN, T. GOLD, H. YARNIS, and R. TURELL. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 290–294, Feb. 14, 1957. 19 refs.

At the Mount Sinai Hospital, New York, 106 native-born Puerto Ricans infected with *Schistosoma mansoni* were examined by means of rectal biopsy, samples of mucosa being taken from the upper half of the rectal ampulla with a bladder punch or angulated cutting forceps. The fragments of mucosa were crushed in a drop of saline and examined microscopically. Stools were also examined, and if no ova were seen, 1 to 2 g. of faeces was concentrated and re-examined.

Of the 106 cases, ova were found in 99 by biopsy and in 88 by stool examination. In 50 cases the average number of ova in the biopsy specimen was 62·7 (range 1 to 400); in 39 of these patients the average number of viable ova was 27 (range 1 to 231), the remaining 11 showing dead ova only. The mucous membrane was generally normal in appearance, and no relationship was observed between the severity of macroscopic damage and the number of ova present. The biopsy technique was more rapid than stool examination, usually only one examination being required, and the condition and morphology of the ova were more easily studied.

[The viability of ova appears to have been judged solely on microscopical appearance, since there is no mention of routine hatching tests. The dosage of stibophen given and the times of examination after treatment are not recorded.] *L. G. Goodwin*

Allergy

600. **Prednisolone Snuff in Hay-fever. A Controlled Trial**

M. P. GODFREY, K. MAUNSELL, and R. S. BRUCE PEARSON. *Lancet* [*Lancet*] **1**, 767–769, April 13, 1957. 8 refs.

In this paper from King's College Hospital, London, details are presented of a small controlled trial in which 46 patients with typical hay-fever, none of whom had received a course of pollen desensitization for at least a year, were paired according to age and sex and treated by inhalation either of prednisolone snuff (Group A) or of an inert snuff (Group B), the actual grouping being revealed only after results had been assessed. A total of 38 patients (18 in Group A and 20 in Group B) completed the trial, which lasted from May 18 to July 7, 1956. Records were kept of the numbers of hay-fever days (H.F.D.) and of 4-mg. tablets of the antihistaminic chlorprophenpyridamine maleate (" piriton ") used (A.T.U.), these tablets being taken as required throughout the period of the trial. The authors point out that the latter formed a better index of the severity of the patients' symptoms than the number of hay-fever days, which merely recorded the presence or absence of symptoms.

The period May 18–31 was used to assess initial severity, and the results from the two groups were very similar, the mean values for Group A being 2·6 H.F.D. and 3·1 A.T.U. per patient, and for Group B 2·7 H.F.D. and 3·2 A.T.U. From June 1 to 30 Group-A patients used capsules for insufflation containing 1 mg. of prednisolone with 144 mg. of lactose, one capsule twice daily, the amount being divided as equally as possible between the nostrils. Group-B patients used similar capsules containing 145 mg. of lactose only. A significant difference ($P=0{\cdot}01$) was found in the number of antihistamine tablets used, though not in the number of hay-fever days: Group A means—7·4 H.F.D., 5·4 A.T.U.; Group B means—14·2 H.F.D., 23·0 A.T.U. Initial difficulty due to blockage of the nose was not encountered, but several patients in Group B complained that the snuff irritated the nose. No side-effects, either local or general, were noted in Group-A patients from the inhalation of prednisolone. During the first week after stopping insufflations (July 1–7) there was no significant difference between the groups: Group A means—1·2 H.F.D., 2·2 A.T.U.; Group B means—3·1 H.F.D., 4·2 A.T.U. The patient's own assessment was determined in every case. Of the 18 patients in Group A, 16 thought the treatment had been " most effective "; 11 out of the 20 patients in Group B said categorically that it had been " no good ". Though a deliberately small dose of prednisolone, one likely to be free from side-effects, was chosen, results compared satisfactorily with those in a group of 18 patients treated by means of pollen desensitization and studied during the same period.

The authors suggest that a more extensive clinical trial of prednisolone inhalation in the treatment of hay-fever is warranted.

H. E. D. Lloyd

601. **Intermittent Positive-pressure Breathing—Aerosol Therapy for Asthma in Children**

R. F. GODDARD and E. H. ROORBACH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 1125–1130, March 30, 1957. 6 figs., 17 refs.

The authors claim that intermittent positive-pressure breathing combined with inhalation of aerosols of various drugs arrests the progress of asthma in children and reverses chronic changes due to oedema, bronchospasm, and emphysema. These methods have been used in the treatment of 100 children between the ages of 1 and 17 years at the Lovelace Clinic, Albuquerque, New Mexico. Respiratory function tests designed to measure the degree of obstruction and abnormalities of diffusion were carried out before and after treatment. Oxygen was delivered with an aerosol spray at a pressure of 10 to 15 cm. of water through a well-fitting face mask for a period of 5 to 10 minutes. The aerosol medicaments used included (1) bronchodilators (isoprenaline, adrenaline), (2) antibiotics, (3) detergents (" alevaire ", " superinone "), and (4) enzymes (crystalline trypsin).

Good results, as judged from clinical evidence and lung function tests, are claimed in 23 of 28 children under 5, 50 of 54 children between 6 and 11 years, and 15 of 18 between 12 and 17 years. A total of 60 to 80 treatments were given in the successful cases, at first daily and later 2 or 3 times weekly over a variable period of time. Striking improvement in the timed vital capacity and nitrogen clearance value was recorded in some cases. In 10% of cases, despite clinical improvement, there was no reversal of pulmonary impairment. One child aged 3 died in an anoxic attack after 15 months of treatment.

No comparable control group was studied, but 40 children with severe asthma who failed to obtain more than temporary improvement with various symptomatic remedies, including steroid therapy, were said to show improvement " of more than a temporary nature " after positive-pressure inhalations. Two-thirds of the successfully treated patients were also having other forms of therapy, including allergic and bacterial immunization and treatment for respiratory tract infections, while 25% were also receiving psychotherapy.

[It is difficult to draw any definite conclusions from this paper. The absence of strict controls and the extensive use of other forms of therapy simultaneously with the positive-pressure treatment are serious criticisms. Nor do the authors give any clear indication of the duration of the treatment or the period over which a follow-up was subsequently conducted.]

R. S. Bruce Pearson

Nutrition and Metabolism

602. **The Intestinal Absorption of Glucose**
R. M. ATKINSON, B. J. PARSONS, and D. H. SMYTH. *Journal of Physiology* [*J. Physiol. (Lond.)*] **135**, 581–589, March 11, 1957. 1 fig., 18 refs.

Experiments were carried out at the University of Sheffield to investigate the fate of glucose absorbed from the intestine *in vivo* and to determine in what form the absorbed glucose appears in the mesenteric blood. Glucose uniformly labelled with radioactive carbon (^{14}C) was introduced into the lumen of an isolated loop of dog intestine. Venous blood from the loop was cooled to prevent glycolysis, led through a dropping chamber, and collected under paraffin to prevent loss of CO_2. About 90% of the radioactive glucose disappearing from the lumen of the intestine could be accounted for in the venous blood, 70% as glucose, 13% as lactic acid, and very small amounts as CO_2, pyruvic acid, and alanine. A comparison with the results of experiments *in vitro* of other workers indicated that *in vivo* a greater fraction of the absorbed glucose was accounted for as glucose and less as lactic acid and CO_2. This was attributed to the rich supply *in vivo* of glucose from arterial blood for oxidative and glycolytic purposes, thus sparing the glucose in the intestinal lumen. *Denis Abelson*

603. **The Glucose Metabolism of Patients with Malignant Disease and of Normal Subjects as Studied by Means of an Intravenous Glucose Tolerance Test**
P. A. MARKS and J. S. BISHOP. *Journal of Clinical Investigation* [*J. clin. Invest.*] **36**, 254–264, Feb., 1957. 1 fig., 39 refs.

The object of this study reported from Columbia University College of Physicians and Surgeons, New York, was to investigate the possible relationship between uncomplicated neoplastic disease and an altered carbohydrate metabolism. There were 19 control subjects, 7 males and 12 females aged 29 to 65 years, and 36 patients with neoplastic disease, 14 males and 22 females aged 36 to 70 years, 14 of whom had clinically localized carcinoma and 22 lymphoma or chronic leukaemia. Strict criteria for selection were employed in both groups, including absence of a family history of diabetes, of any disorder known to affect carbohydrate metabolism, and of fever. Histological confirmation was obtained in all cases of neoplastic disease and the subjects were studied before treatment.

After 2 weeks on standard diet with an adequate carbohydrate content an intravenous glucose tolerance test was performed by a standardized technique, being repeated on 2 or 3 occasions in 10 cases. Two types of glucose tolerance curve were obtained: (1) by plotting the logarithm of the total blood sugar concentration against time, and (2) by plotting the logarithm of the blood sugar concentration in excess of the fasting value against time. These two methods allow the glucose tolerance curve to be analysed in terms of a single constant and the results can be compared with normal data available in the literature. Moreover, in the present study they were found to be readily reproducible, in any individual.

There was no significant difference in the mean fasting blood sugar concentration between the two groups, but there was a significant decrease in the glucose tolerance of patients with malignant disease as indicated by diminution in both the fractional rate and the net rate of disappearance of glucose. There was no significant difference in the estimated volume of distribution of glucose between the two groups. The authors suggest that these findings might be due to a greater net hepatic glucose output or a decrease in peripheral utilization, or a combination of the two, in subjects with neoplastic disease. Peripheral glucose utilization is associated with a fall in serum inorganic phosphate level together with a decrease in serum potassium concentration and is related quantitatively to these changes. Although no significant difference was found between the two groups in respect of the maximum fall of serum inorganic phosphate and potassium levels, the fasting serum inorganic phosphate level was higher and the percentage fall significantly less in the neoplastic group than in the control group. It is suggested that this might reflect alterations in host tissue metabolism.

It is concluded that the defect of carbohydrate metabolism in malignant disease is non-specific, but that its study may shed some light on metabolic alterations associated with neoplastic processes. *B. M. Ansell*

604. **Sodium Balance Studied with ^{22}Na and an External Counter for Measuring Whole-body Radioactivity**
M. M. MARTIN, G. WALKER, and M. CHAPMAN. *Lancet* [*Lancet*] **1**, 653–656, March 30, 1957. 3 figs., 6 refs.

In a study carried out at the Middlesex Hospital, London, serial measurements of the total exchangeable body sodium were made in 6 patients over periods of 13 to 26 days, 25 μc. of radioactive sodium (^{22}Na; half-life 2·6 years) being used as tracer. Comparison was made between two different methods of estimating total body sodium: (1) that based on the dilution of ^{22}Na in the extracellular fluid and corrected for day-by-day losses in the urine and faeces (the cumulative excretion method); and (2) that based on the use of an external body counter, which in this study was constructed from 4 matching Geiger–Müller tubes mounted on a trolley low enough to fit beneath a hospital bed. Method 2 has the advantage of requiring neither measurement of sodium intake nor the collection of excreta.

Equilibration of the radioactive tracer with the body sodium content was obtained in from 3 to 5 days. The accuracy of an individual measurement of exchangeable sodium was found to be $\pm 2{\cdot}4\%$. In 5 out of the

6 subjects the cumulative excretion method showed a greater gain or smaller loss of body sodium than the external counting method. The differences, however, were small and could have been accounted for by a small daily loss of sodium in the sweat, which is not measured by the former method. *E. Keith Westlake*

METABOLIC DISORDERS

605. **Renal Excretion of Phosphorus in Pseudohypoparathyroidism. Observations on the Effects of Probenecid and Acetazoleamide in Two Patients**

K. B. Baer, T. Benedek, I. Rosenthal, and H. J. Zimmerman. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **99**, 14–21, Jan., 1957. 7 figs., 21 refs.

In this paper from West Side Veterans Administration Hospital, Chicago, the authors describe the effect of probenecid and acetazolamide on 2 patients with pseudohypoparathyroidism. In the first case, that of a man aged 30, administration of parathyroid extract did not result in increased excretion of phosphate, although there was a twelvefold increase in a control subject. The second patient, a female, also failed to respond to parathyroid extract, but so did 2 controls. Electrophoresis of the serum proteins revealed an increase in the γ-globulin level in both patients.

In the male patient a marked phosphaturia occurred after administration of probenecid, but a second course was less effective; no response was obtained in the female. The response to acetazolamide administration in both patients resembled that to probenecid. In view of these findings the authors consider neither drug to be suitable for the treatment of pseudohypoparathyroidism.

Denis Abelson

606. **5-Hydroxytryptamine Deficiency in Phenylketonuria**

C. M. B. Pare, M. Sandler, and R. S. Stacey. *Lancet* [*Lancet*] **1**, 551–553, March 16, 1957. 39 refs.

A quantitative examination of the metabolic pathway of 5-hydroxytryptamine (5-HT) in phenylketonuric subjects was undertaken by the authors at a number of London hospitals to see whether there was a failure of hydroxylation of tryptophan similar to that of phenylalanine. Serum 5-HT was estimated by allowing blood to stand in the incubator for one hour at 37° C. and then separating the serum by centrifugation. The 5-HT was extracted with 95% acetone and assayed on the rat uterus. Brom-lysergic acid was used as an antagonist in a concentration of 50 nanogrammes per ml. in order to test for the presence of other smooth-muscle-stimulating substances. Four groups of children were investigated: Group I—12 healthy children aged 3 to 12 years living at home, in whom only urinary 5-hydroxyindoleacetic acid (5-HIAA) was measured; Group II—15 children in hospital awaiting tonsillectomy; Group III—10 phenylketonuric subjects; Group IV—9 mentally defective children without phenylketonuria. The children with phenylketonuria showed significantly lower values for serum 5-HT and urinary 5-HIAA; low serum 5-HT values were associated with normal platelet counts. No correlation was found between the I.Q. and serum 5-HT and urinary 5-HIAA in phenylketonurics. The urinary 5-HIAA of children awaiting tonsillectomy was considerably higher than that of normal children living at home. Some non-phenylketonuric mental defectives had surprisingly high serum 5-HT levels.

The authors discuss the relationship of these findings to phenylketonuric mental deficiency.

Norval Taylor

607. **Intermittent Aldosteronism in Periodic Paralysis. Dependence of Attacks on Retention of Sodium, and Failure to Induce Attacks by Restriction of Dietary Sodium**

J. W. Conn, L. H. Louis, S. S. Fajans, D. H. P. Streeten, and R. D. Johnson. *Lancet* [*Lancet*] **1**, 802–805, April 20, 1957. 6 figs., 21 refs.

The part played by sodium retention in precipitating attacks was studied at the University of Michigan, Ann Arbor, in two young men with the familial type of periodic paralysis. One of them was investigated over a period of 11 months, the other for 30 days. Two levels of sodium intake—8 and 208 mEq. per day—were used. Potassium intake was kept constant at 132 mEq. per day. Under both sets of dietary conditions experiments designed to induce episodes of periodic paralysis were carried out. When the diet contained the larger quantity of sodium the administration of glucose, insulin, or 2-methyl-9-α-fluorohydrocortisone produced complete and prolonged paralysis. In each case the urinary and serum potassium levels fell sharply, but this was always preceded, and then accompanied, by intense sodium retention. When the diet was low in sodium, attacks of paralysis could not be induced by these procedures and potassium retention did not occur. Skeletal muscle obtained during the period of high sodium intake contained an excessive amount of sodium and a normal or slightly subnormal concentration of potassium, and histological changes characteristic of the disease were present. In skeletal muscle after 44 days on the low sodium diet the histological changes had disappeared.

It is suggested that retention of sodium is the primary factor which sets in motion the characteristic chain of events in an episode of periodic paralysis.

H. Harris

608. **Absorption of Water and Sodium from the Small Intestine of Patients with Nontropical Sprue**

J. A. Higgins, P. R. Lee, J. F. Scholer, R. J. Reitemeier, C. F. Code, and E. E. Wollaeger. *Journal of Clinical Investigation* [*J. clin. Invest.*] **36**, 265–269, Feb., 1957. 14 refs.

Using recently developed methods for the determination of the rates of absorption of isotopically labelled substances from the gastro-intestinal tract the authors, working at the Mayo Clinic, have investigated the absorption of water and sodium in cases of non-tropical sprue. Dual isotopes of water (deuterium and tritium oxide) and of sodium (^{22}Na and ^{24}Na) were employed. Tests were carried out on 14 patients, 3 males and 11

females aged 23 to 63 years, with typical non-tropical sprue, most of them while the patients were in relapse, though in 6 cases tests were made during a remission. All observations were made with the patient in the fasting state, the isotope or isotopes, together with 10 g. of barium sulphate, being introduced into the third part of the duodenum by means of a Sawyer tube. The rate of absorption of water alone was measured 8 times in 5 subjects and of water and sodium together in the remaining subjects, the rate of absorption of an isotope being calculated by integration of the rate of its appearance in the arterial blood after administration into the duodenum, and the rate of its disappearance from the arterial blood after rapid intravenous injection At the outset these rates were determined separately, but in the last 5 instances dual isotopes were employed and the rates measured simultaneously.

In comparison with normal individuals previously studied by the same method all patients in whom water absorption alone was studied during a relapse showed a slow rate of absorption, the degree of slowing being related to the clinical state. Of the patients on whom simultaneous determinations of water and sodium were made, water absorption was again slower in those in relapse, becoming more nearly normal when the patients were in remission. The rate of absorption of sodium was even more decisively retarded in all but one patient, who at the time of study was in remission. Again there was correlation between the severity of the clinical state and degree of retardation of absorption. All the patients showed a slow spread of barium throughout the intestine, often with puddling.

Although it is realized that the method here employed measures unidirectional flow rather than exchange, the retardation of water absorption demonstrated is in agreement with the findings of other workers. This is likely to be due in part to reduced intestinal motility, but it is suggested that as defective absorption of sodium is even more marked than that of water, other and more specific defects are probably involved. *B. M. Ansell*

609. **The Effect of a Gluten-free Diet on Fat, Nitrogen, and Mineral Metabolism in Patients with Sprue**
M. K. Schwartz, M. H. Sleisenger, J. H. Pert, K. E. Roberts, H. T. Randall, and T. P. Almy. *Gastroenterology* [*Gastroenterology*] **32**, 232–246, Feb., 1957. 2 figs., 31 refs.

Six adults, chronically ill with idiopathic steatorrhoea, showed marked clinical improvement within several weeks of starting a gluten-free diet in all cases, diarrhoea disappearing and the stools becoming normal in appearance. Blood calcium, albumin, and prothrombin levels returned to normal. Gluten flour, 3 g. daily, was given to 4 patients by the " double-blind " method after they had returned to normal. In 2 cases there was no adverse effect in 3 weeks, and in one case diarrhoea occurred in one week; the remaining patient, who also ate a gluten-containing diet, had diarrhoea with abdominal distress and anorexia within a week.

Detailed metabolic studies were carried out on 2 patients before and during the administration of a gluten-free diet. Fat absorption, initially 35% and 54% respectively, became normal (94%) in 2 to 3 months. One patient, after 8 months on the diet, resumed a normal diet. Fat absorption fell to 76% in one week and diarrhoea returned. Faecal nitrogen loss fell from 3·6 g. per day before taking the diet to 0·9 g. per day during the diet in one case; the corresponding figures for the other patient were 2·8 g. and 1·6 g. per day. In each case nitrogen balance was positive before and during the diet. Faecal calcium, phosphorus, sodium, and potassium levels were all high before the gluten-free diet and fell to normal values during the diet period. Sodium and potassium loss in the faeces rose slightly in the case of the patient who resumed a normal diet, but calcium and phosphorus loss was even less. The faecal magnesium content was reduced in one patient as a result of the gluten-free diet and rose in the other. There were no side-effects of the gluten-free diet. The authors suggest that it should always be tried first in the treatment of idiopathic steatorrhoea, and steroid therapy instituted only when it fails. *M. Lubran*

610. **Acute Recurrent Rhabdomyolysis (Paroxysmal Myohemoglobinuria). A Report of Three Cases and a Review of the Literature**
D. H. Bowden, D. Fraser, S. H. Jackson, and N. F. Walker. *Medicine* [*Medicine (Baltimore)*] **35**, 335–353, Dec., 1956 [received April, 1957]. 4 figs., 46 refs.

In this paper from the Hospital for Sick Children, Toronto, a simple method is described for discriminating between oxyhaemoglobin and oxymyohaemoglobin, an ordinary fluorescent lighting tube and standard direct-vision hand spectroscope being used. The findings in 25 cases of paroxysmal myoglobinuria reported in the literature are reviewed, and 3 further cases are described. One of the patients, a boy of 4 years, died suddenly. In most of the organs no gross abnormality was observed at necropsy, but histological examination of the muscles suggested that severe acute muscle damage had occurred. In the other 2 cases it was possible to follow certain biochemical changes during an attack. Urinary excretion of creatine was extremely high during the acute phase and then fell below normal as the attack subsided. A year later the urinary excretion was normal. The early increase in creatine excretion is interpreted as evidence of a sudden liberation of muscle constituents into the blood stream, and the subsequent period of diminished concentration as evidence of depletion of muscle phosphocreatine stores. Urinary excretion of creatinine was slightly reduced in the acute phase, but soon became normal. The blood glycogen level was raised during the acute attack, possibly because of liberation of muscle glycogen. No change in the serum potassium level was observed. In one case there was marked amino-aciduria during the attack.

It is suggested that during the acute phase a number of different substances, one of which is myoglobin, are liberated into the blood stream by lysis of striated muscle. It is suggested that a more appropriate name for the disease would be acute recurrent rhabdomyolysis.

H. Harris

Gastroenterology

STOMACH AND DUODENUM

611. **A Study of *X*-ray Negative Dyspepsia with Reference to Histologic Changes in the Gastric Mucosa**
M. SHINER and I. DONIACH. *Gastroenterology* [*Gastroenterology*] **32**, 313–324, Feb., 1957. 4 figs., 12 refs.

At the Postgraduate Medical School of London the authors examined the histological appearance of biopsy specimens of gastric mucosa in 50 cases in which no ulcer could be demonstrated histologically, in 19 cases of proven peptic ulcer (9 gastric and 10 duodenal), in 15 cases of pernicious anaemia, in 7 cases of iron-deficiency anaemia, and in 9 control subjects without gastrointestinal symptoms. The importance is stressed of obtaining more than one biopsy specimen and of repeating the examination in order to get a true picture of the mucosal histopathology. Four types of appearance are described, with illustrations: (1) normal mucosa; (2) gastritis without gross atrophy; (3) partial atrophic gastritis; and (4) subtotal gastric atrophy.

Of the 50 cases of dyspepsia with negative *x*-ray findings, normal mucosa was present in 33, gastritis in 8, partial atrophic gastritis in 8, and subtotal gastric atrophy in one. Of the 19 cases of peptic ulcer, normal mucosa was present in 7 (3 with gastric and 4 with duodenal ulcer), gastritis in 11 (6 with gastric and 5 with duodenal ulcer), and subtotal gastric atrophy in one case of duodenal ulcer. Of the 15 cases of pernicious anaemia, partial atrophic gastritis was present in one and subtotal gastric atrophy in 14. Of the 7 cases of iron-deficiency anaemia, normal mucosa was present in one, partial atrophic gastritis in 3, and subtotal gastric atrophy in 3. The 19 cases of subtotal gastric atrophy were histologically indistinguishable from one another. The 2 cases in the dyspeptic groups were not associated with anaemia, and of the 17 cases in the non-dyspeptic groups, only in one did the patient volunteer a history of dyspepsia. The authors draw special attention to these cases as they believe that whatever its aetiology, subtotal gastric atrophy may possibly be a pre-cancerous condition.

A careful comparison was made between the clinical features of *x*-ray negative and *x*-ray positive dyspepsia, with particular reference to the presence and character of pain, its duration, periodicity, relation to meals, and relieving factors, and the presence or absence of nocturnal pain, vomiting, anorexia, weight loss, flatulence, and history of haematemesis or melaena. There was very little difference between the 2 groups except that in the former tenderness was less localized and pain occurred sooner after meals; flatulence occurred twice and haematemesis half as often in the radiologically negative cases as in those of proved peptic ulcer. Histological comparison showed that in both dyspeptic groups there was a progressive increase in abnormal pathology in the gastric mucosa with advancing years. In neither was there any correlation between histology and vomiting or loss of weight.

In the group with *x*-ray negative dyspepsia the history of pain was, on average, twice as long in patients with partial atrophic gastritis and subtotal gastric atrophy as in those showing normal mucosa or gastritis without gross atrophy, but there was no correlation between the histological findings and either the severity of the pain or the time of its onset in relation to meals; in 20 cases the pain bore no relation at all to meals. Flatulence and loss of weight were more common when the mucosa showed gastritis without gross atrophy, and a history of haematemesis was confined to patients showing normal histology at the time of biopsy. The free and total acid and pepsin content of the gastric juice was normal in patients with healthy mucosa or with gastritis, but subnormal in those with partial atrophic gastritis and subtotal gastric atrophy. Gastroscopic findings (in 19 patients) were seldom in agreement with the histological picture or the gastric pepsin or acid estimations.

E. S. Wyder

612. **The Etiology of Experimental Gastric Ulceration**
J. D. WEISZ. *Psychosomatic Medicine* [*Psychosom. Med.*] **19**, 61–73, Jan.–Feb., 1957. 18 refs.

This study was designed with the primary purpose of testing two hypotheses: (1) animals placed in a severe conflict situation for a relatively long period of time (30 days) would develop gastrointestinal changes which would lead to the formation of gastric ulcers; (2) animals placed in a chronic fear-producing situation for a relatively long period of time (30 days) would develop gastrointestinal changes which would lead to the formation of gastric ulcers. To test these hypotheses, 90 rats were divided into 6 split-litter groups (insofar as possible), of equal size, and each of these groups was placed in a different experimental situation. Two of these situations subjected the animals to an approach-avoidance type of conflict; two situations were fear-producing, with food and water deprivation being present in one of these but not in the other; and two were control situations involving only food and water deprivation or food and water deprivation plus cephalic phase (seeing and smelling food and water). During testing, 30 of the animals were on a 46-hour deprivation schedule and 45 animals were on a 47-hour deprivation schedule. Fifteen animals in one of the fear-producing situations were not deprived of food and water.

With respect to the two hypotheses the following conclusions were reached by the author. (1) A significantly greater number of animals in the two conflict situations developed lesions in the rumen of their stomachs than the comparable animals in the two control situations. This evidence was interpreted as confirming the first hypothesis. (2) A significantly greater number of animals in one of the fear-producing situations (also

involving deprivation) developed lesions in the rumen of their stomachs than the animals of the appropriate control situation. This evidence was interpreted as supporting the second hypothesis. (3) A significantly larger number of animals of the fear-producing situation (in which deprivation was present) had Stage 2 changes than those of the fear-producing situation in which food and water was always present. These results were interpreted as indicating that having the animals on a severe food- and water-deprivation schedule seemed to be a necessary prerequisite for the occurrence of the lesions in the rumen of the stomach. (4) The presence of the cephalic phase variable (present in two situations) was associated with a slight but insignificant increase in the relative frequency of lesions in the rumen of the stomach. The interpretation here was that the more severe gastric trauma observed in these situations could not be attributed to the presence of the cephalic phase variable since similar pathological changes were observed in the situations where this variable was not present. (5) Conflict and chronic fear as induced in this investigation seem to be associated with similar frequencies of pathological changes.

It was postulated that either an excessive volume of gastric juice or an increase of its acidity brought about the lesions, and that these gastrointestinal changes occurred to a large extent as a result of the induced conflict or fear states.—[From the author's summary.]

613. **" Stress " Ulceration of the Gastro-intestinal Tract. Clinical Characteristics**

B. G. GRIFFIN, L. R. LAWSON, and D. L. MOORE. *Gastroenterology* [*Gastroenterology*] **32**, 404–414, March, 1957. 38 refs.

In this paper from the Hermann and Jefferson Davis Hospitals, Houston, Texas, 9 cases of acute peptic ulcer occurring as a sequel to trauma or severe acute illness are reported. Curling in 1842 first described this type of peptic ulceration after burns. The condition was found in 2 out of 300 consecutive necropsies, an incidence of 0·66%. Gastro-intestinal haemorrhage was present in all 9 cases in the present series, and in one perforation occurred. The interval between the initial trauma and the occurrence of acute haemorrhage varied from 3½ hours to 2 months. Abdominal pain or dyspepsia was a common symptom. The trauma was to the central nervous system in 4 instances, including one in which there was subarachnoid haemorrhage. Neoplastic or vascular disease of the nervous system was present in 3 cases, abscess of the appendix in one, and carcinomatosis in one.

The clinical management of these cases is similar to that of other cases of acute gastro-intestinal haemorrhage; in one patient an emergency partial gastrectomy was successful in eliminating an acute ulcer eroding an arteriole. The mechanism of the production of the ulceration is discussed. The authors' findings emphasize the importance of being aware of the signs of gastro-intestinal haemorrhage in any patient with a severe acute illness, particularly after trauma to the central nervous system. *I. McLean Baird*

614. **Etiology of Duodenal Ulcer—I. Relation of Specific Psychological Characteristics to Rate of Gastric Secretion (Serum Pepsinogen)**

H. WEINER, M. THALER, M. F. REISER, and I. A. MIRSKY. *Psychosomatic Medicine* [*Psychosom. Med.*] **19**, 1–10, Jan.–Feb., 1957. 1 fig., 22 refs.

The authors describe a study planned to evaluate the role of gastric hypersecretion, psychic tension, and environmental factors in the production of duodenal ulceration which was carried out at the Walter Reed Army Institute of Research, Washington, D.C., and the University of Pittsburgh, Pennsylvania. Levels of serum pepsinogen were estimated in 2,073 army draftees, aged 17 to 29 years, chosen at random; of these, 120 were selected for further special study because they were in the range of the highest and lowest values obtained. Before being sent to the basic training area each subject was examined by several psychological tests [which are listed] and had complete *x*-ray examination of the upper alimentary tract. Of this group, 107 had further psychological tests and *x*-ray study after 8 to 16 weeks of the basic training period.

The second *x*-ray examination showed active duodenal ulcer in 5 men with a high pepsinogen level who had a normal radiograph at the outset of the study. The results of the psychological tests alone were studied in an attempt to correlate mental traits with gastric secretion; this showed that 71% of the hypersecretors and 51% of the hyposecretors were correctly designated. To develop a more accurate diagnostic method a *post hoc* study was made of 20 criteria from the psychological test material. On the basis of these data 85% of the 120 men could be correctly classified as hypo- or hypersecretors. The subjects with peptic ulcer showed evidence of major unresolved conflicts about dependency and oral gratification, the characteristics of which are described.

The authors conclude that neither gastric hypersecretion nor a specific personality trait is alone responsible for the production of duodenal ulcer, but that these are essential predisposing factors in the individual who develops a peptic ulcer in noxious environmental circumstances. *T. J. Thomson*

615. **Observations on the Value of Gastric Irradiation in the Treatment of Duodenal Ulcer**

E. LEVIN, C. B. CLAYMAN, W. L. PALMER, and J. B. KIRSNER. *Gastroenterology* [*Gastroenterology*] **32**, 42–49, Jan., 1957. 9 refs.

In this paper from the University of Chicago the results of gastric irradiation in the treatment of duodenal ulcer in 723 patients over a period of almost 20 years are reported. In nearly all cases the diagnosis was confirmed radiologically. Radiotherapy, the purpose of which is to diminish excessive acid secretion, was used in addition to the usual treatment with rest, strict diet, and antacids. The dosage before 1939 varied from 600 to 3,600 r (measured in air). Between 1939 and 1944 the depth dosage varied from 1,100 to 1,500 r, and after 1944 from 1,600 to 1,700 r, given over 10 to 14 days. In a few cases a second course was given months or

years later. After discharge all the patients were kept under observation either as out-patients or they were followed up by telephone or postal inquiry for 6 to 18 years.

Gastric secretion was shown to have decreased by over 50% 2 to 4 weeks after irradiation in 258 patients (36%). This decrease persisted for 6 to 12 months in 12% patients and for 1 to 18 years in 135 patients. Histamine achlorhydria developed in 85 patients (12%), but was transient in most cases, small quantities of hydrochloric acid being detected in the gastric juice within 6 months of treatment in 66 patients. In each instance the ulcer healed and did not recur during the period of achlorhydria, recurrences in this group being invariably preceded by a return of the hydrochloric acid secretion to previous levels.

It is claimed that both the frequency and the severity of recurrences were considerably reduced by this treatment [though the absence of controls reduces the weight of this claim]. Of the 723 patients treated, recurrences occurred in 332 (46%), the interval between treatment and recurrence being less than 12 months in 126, while 11[illegible] patients (16%) ultimately required surgery. Of the 33[illegible] patients who experienced recurrence, 225 (64%) indicated that their symptoms were much milder than those present before treatment, and 116 of these 225 lost the symptoms after a temporary resumption of medical treatment, after which no further recurrences were observed. Of the 723 patients, 259 had had one or more haemorrhages before therapy, whereas only 40 suffered haemorrhage after therapy. The incidence of haemorrhage was 4·3 per 100 patient-years before and 1·1 per 100 patient-years after treatment—a reduction of 75%.

There were 8 deaths from causes connected with the ulcer (4 from haemorrhage, 3 from acute perforation, and one from myocardial infarction following surgery for ulcer). In addition there were 4 deaths from cancer of the stomach (which in 2 cases was thought to have been present at the time of treatment), 4 from carcinoma of the pancreas, and one from primary cancer of the liver. Radiation injury was insignificant except for one case of necrosis in the left lobe of the liver, which was followed by complete recovery. *F. S. Freisinger*

616. **Preliminary Trial of Cerebral Surgery in the Treatment of Resistant Gastric and Duodenal Ulcers.** (Premières tentatives chirurgicales sur le cerveau pour le traitement des ulcères gastriques et duodénaux rebelles) P. FRUMUSAN, R. CATTAN, and M. BUCAILLE. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **33**, 521–533, Feb. 10, 1957. 12 figs., 29 refs.

The relation between organic cerebral lesions and the peptic-ulcer syndrome is reviewed, and it is pointed out that such lesions usually produce acute erosions and are not found in chronic cases. For the healing of the ulcer psychosomatic rest is considered important and may be achieved surgically by interruption of cortico-hypothalamic fibres in the prefrontal region by procaine infiltration or electrocoagulation. Of 5 patients operated on at the Hôpital Saint-Antoine, Paris, between 1953 and 1955, one was treated in this way rather than by gastrectomy for unexplained melaena, found later to be due to a duodenal ulcer, while the others had received one to 5 years of medical treatment combined with rest in bed [if the energetic measures described permitted rest] without permanent benefit. There were no operative deaths: in one case epilepsy developed after procaine infiltration and the gastric condition relapsed, requiring gastrectomy, and in one there was reactivation of pulmonary tuberculosis. The results in the other 3 cases after 2 to 3 years' observation seem on the whole satisfactory.

[This paper should be read in the original for a detailed description of the techniques used by the authors. It is probable that most British and American neurosurgeons would doubt the possibility of stabilizing a surgical technique which uses bony landmarks only, and would prefer leucotomy, although this involves opening the dura. In cortical atrophy, for example, the abstracter is reliably informed that this may be essential. Neurosurgery might be of value in the treatment of intractable post-gastrectomy symptoms.] *W. A. Bourne*

PANCREAS

617. **Value of Combined Study of Serum Enzymes and Duodenal Contents after Secretin in the Diagnosis of Diseases of the Pancreas**
D. C. H. SUN and H. SHAY. *Gastroenterology* [*Gastroenterology*] **32**, 212–231, Feb., 1957. 27 refs.

A combined study of changes in the serum amylase and lipase concentrations and in the volume and bicarbonate concentration of the duodenal contents after stimulation of the pancreas with secretin has been carried out at Temple University School of Medicine, Philadelphia, with the aim of establishing the basis for an adequate test of pancreatic function. In 87 normal subjects the mean serum amylase concentration (in terms of the amount of glucose liberated from starch by 100 ml. of serum) was 100 mg. (S.D. 31 mg.), the upper limit of normal being 193 mg. In 96 normal subjects the mean serum lipase concentration (in terms of the amount of N/10 sodium hydroxide solution required to neutralize the acid produced by the action of 1 ml. of serum on olive oil) was 0·16 ml. (S.D. 0·08 ml.), the upper limit of normal being 0·4 ml.

Serum amylase and lipase concentrations were then determined in 10 normal subjects before and 1, 2, and 4 hours after the intravenous injection of 10 ml. of normal saline, and in 30 normal subjects and 36 patients with pancreatic disease at similar intervals after the intravenous administration of 80 units of secretin. In many cases duodenal juice was obtained by intubation during the same period. All serum amylase and lipase levels were within normal limits in the control subjects receiving saline and in those receiving secretin. In 20 of the latter the duodenal juice was examined, the mean total volume in one hour after secretin administration being 2·5 ml. per kg. body weight (S.D. 0·42 ml.) and the mean maximum bicarbonate concentration 97·0 mEq.

per litre (S.D. 14·0 mEq.). In 5 out of 7 cases of acute pancreatitis the fasting serum amylase and lipase levels were normal and in 4 of these there was an increase in the level of one or both of the enzymes after secretin administration. The duodenal juice was normal in both volume and bicarbonate content in these 4 and was not examined in the fifth. In the remaining 2 cases of acute pancreatitis the fasting level of one or both of the enzymes was above normal and showed no further increase with secretin; in one of these both volume and bicarbonate content of the duodenal juice were below normal and in the other the bicarbonate content was reduced.

Of 12 cases of chronic pancreatitis, the fasting serum enzyme concentrations were normal in 7, and secretin produced a rise in level in 4 of these. In the other 5 cases, in which the fasting levels were above normal, a further rise was produced by secretin. The volume or bicarbonate content of the duodenal juice, or both, was reduced in all 12 cases. The test was also carried out on 5 patients with gall-stones or peptic ulcer and symptoms suggestive of pancreatic involvement. In all cases the fasting serum enzyme levels were normal, but secretin produced a significant rise in one or other or both, while in 4 cases the duodenal juice was abnormal. In 7 out of 12 patients with proved carcinoma of the pancreas the fasting amylase and lipase levels were normal and only in one of these was there a positive response to secretin. The duodenal juice was examined in 4 of these cases and showed a significant decrease in volume or bicarbonate content or both in all 4. The remaining 5 patients with carcinoma had raised fasting serum enzyme levels and a further rise occurred with secretin in 3 cases. Abnormality of the duodenal contents was found in the 3 cases in which they were examined.

The authors consider the combined test to have some value in the investigation of pancreatic disease and suggest the interpretations which should be put on various combinations of findings. [However, its value as a diagnostic test for pancreatic disease seems doubtful on the basis of the evidence presented in this paper.]

M. Lubran

LIVER

618. **Parotid Swelling, Alcoholism and Cirrhosis**
S. J. WOLFE, W. H. J. SUMMERSKILL, and C. S. DAVIDSON. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 491–495, March 14, 1957. 3 figs., 22 refs.

Asymptomatic non-inflammatory enlargement of the parotid glands associated with severe liver failure was seen in 16 patients (9 males and 7 females aged 29 to 67 years) at the Boston City Hospital. With one exception the patients had been chronic alcoholics for many years, and at the time of admission were considered to be suffering from severe cirrhotic changes. In all cases there was a history of dietary insufficiency.

A review of the literature revealed that similar enlargement of the parotid glands occurs in association with malnutrition in other conditions. *John Fry*

619. **The Recognition and Differential Features of Indirect Reacting Hyperbilirubinemia**
S. REICHMAN and W. D. DAVIS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 523–536, March, 1957. 2 figs., 10 refs.

The differential diagnosis of continuing jaundice in servicemen who have been exposed to epidemics of hepatitis is discussed in this paper from the U.S. Naval Hospital, Portsmouth, Virginia. Confusion may arise from the occurrence amongst them of cases of congenital haemolytic icterus and constitutional hepatic dysfunction, which superficially resemble viral hepatitis. In both these conditions, however, most of the liver function tests give normal results; moreover, the bilirubin accumulating in the serum is of the indirect-reacting type. Other distinctive features of these conditions are discussed with reference to illustrative case records.

J. McMichael

620. **Observations of Liver Function in Chlorpromazine-treated Alcoholic Patients**
M. D. SMALL, A. E. LONGARINI, and N. ZAMCHECK. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 932–934, May 16, 1957. 13 refs.

621. **Hepatography with Radioactive Gold.** (Hepatographie mit radioaktivem Gold)
H. R. RENFER, G. G. PORETTI, C. MASSINI, and A. ZUPPINGER. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **87**, 255–259, March 16, 1957. 9 figs., 8 refs.

In this communication from the University of Berne the authors describe the technique of hepatography with radioactive gold (^{198}Au), which they have found useful in detecting tumour metastases in the liver and in the differential diagnosis of epigastric tumours. It consists essentially in mapping the radioactivity recorded over the lower thoracic and upper abdominal areas 2 hours after the intravenous injection of 500 μc. of colloidal ^{198}Au. At this time some 75 to 85% of the active material has been taken up in the reticuloendothelial system of the liver; allowing for natural decay of radioactivity this level is maintained for 48 to 96 hours.

In carrying out the procedure the patient is positioned in relation to standard anatomical surface features under a fully automatic scanner which carries the scintillation tube and collimator. Respiratory excursion is minimized by giving pure oxygen to breathe and by applying an abdominal binder. As it is essential for the patient to remain completely still during the examination the couch should be comfortable, coughing suppressed with a suitable drug, and any ascitic fluid should be drawn off the previous day. Selected anatomical landmarks are first drawn on the record and this is then correctly aligned under the writing level of the scanning apparatus. Conditions of scanning speed and other factors are chosen to give optimum resolution of the record; it is stated that with a collimator width of 9 mm., "a scale of 16", and a pen speed of 2 mm. per second, 10 to 12 marks per cm. are recorded over the zones of highest radioactivity. The whole examination takes up to 90

minutes. The completed hepatogram consists of rows of short vertical pen marks on the paper, these being sometimes close together, sometimes more widely separated, giving the effect of shading, so that a visual picture in relation to the anatomical landmarks is presented on the record. [This is very clearly seen in the illustrations accompanying the paper.]

In normal subjects the hepatogram has a relatively regular pattern. In patients with hepatic involvement areas corresponding to metastases in the liver show up as defects and irregularities in this pattern; the latter reflect the situation in the reticuloendothelial tissue of the liver only. Metastases measuring 5 cm. in diameter or more are well defined, those of 3 cm. diameter may be detectable in favourable circumstances, but lesions under this size are not recorded. The radiation hazard of the technique is discussed. The dose to the relatively sensitive liver tissue is considered to be within reasonable limits for a diagnostic procedure. The main indications for use of this method are the demonstration of metastases in the upper half of the liver and of hepatic abscesses, and the technique may also have some application in the differential diagnosis of tumours of the right hypochondrium or subphrenic area. The authors, while admitting certain limitations, hope that with improved technique better resolution may be possible and the radiation hazard to the patient may be reduced by using other isotopes. [Clearly the value of the technique is limited by the large size (3 cm.) of the smallest metastases which can be detected with certainty by the existing apparatus.] *Derek R. Wood*

622. **Analysis of Causes of Death in Laennec's Cirrhosis**
G. GHASE, C. MARTEL, and R. OLIVETTI. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] 233, 259–263, March, 1957. 9 refs.

This is a brief review which is concerned mainly with changes in the causes of death in cases of cirrhosis of the liver in recent years. The authors first analyse the causes of death in 66 cases of hepatic cirrhosis which came to necropsy at the Veterans Administration Hospital, Newington, Connecticut, between the years 1947 and 1955. These cases constituted 6·4% of all necropsies during that period, and in every instance there was a history of alcoholism. Death was due to hepatic insufficiency in 44%, haemorrhage in 38%, pneumonia in 4·5%, and miscellaneous causes in 13·5%. These figures are contrasted with those given by Evans and Gray in 1938 and by Cates [year not specified], the main difference being the great diminution in deaths from pneumonia and intercurrent infections, which made up 37% of the former and 30% of the latter series, but only 4·5% of the present series. This change in the natural history of hepatic cirrhosis associated with alcoholism is attributed to the advent of antibiotic therapy. *J. W. McNee*

623. **Prednisone Treatment in Cirrhosis of the Liver.** [In English]
K. WINKLER and N. TYGSTRUP. *Acta medica Scandinavica* [*Acta med. scand.*] **157**, 149–156, March 25, 1957. 3 figs., 21 refs.

INTESTINES

624. **A Study of 356 Carcinoids of the Gastrointestinal Tract. Report of Four New Cases of the Carcinoid Syndrome**
R. A. MACDONALD. *American Journal of Medicine* [*Amer. J. Med.*] **21**, 867–878, Dec., 1956. Bibliography.

The author discusses the natural history of gastrointestinal carcinoids and their possible association with 5-hydroxytryptamine, and then analyses a series of 356 cases found in the records of 7 hospitals in Boston. Of the 356 tumours, 149 were extra-appendiceal and 207 appendiceal, and the authors emphasize the importance of differentiating between these two types.

Altogether 146 of the 149 extra-appendiceal cases could be graded as follows: 33% were non-invasive, 27·3% had invaded muscle coats only, 23·3% had spread to regional lymph nodes, and 16·4% had metastasized to distant organs, mainly to the liver and lung. The tumour was of proved multiple origin in 16% of the series of 149. Of the 207 appendiceal carcinoids, only 11% showed any evidence of invasiveness; in none of the cases was there spread to distant organs. The so-called carcinoid syndrome was found in 4 of 21 cases of widespread metastasis, the main clinical features being watery stools, flushing, a reddish-violet rash, and pulmonary stenosis.

The author recommends local resection in cases of non-invasive extra-appendiceal carcinoids and resection with local lymph-node dissection in cases of invasive tumours, even in the presence of wide-spread metastases, as obstruction at the primary tumour site may occur. In cases of appendiceal carcinoids appendicectomy " should be adequate ". *R. Schneider*

625. **Indications for and Results of Prefrontal Surgery in Ulcerative Colitis.** (Indications et résultats dans interventions pré-frontales dans les recto-colites ulcéro-hémorragiques)
R. CATTAN, R. CARASSO, P. FRUMUSAN, P. NATAF, R. SOUPAULT, and M. BUCAILLE. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] 33, 507–521, Feb., 1957. 10 figs., 3 refs.

From the Hôpital Saint-Antoine, Paris, the treatment of 12 cases of ulcerative colitis, 5 by infiltration with procaine and the remainder by electrocoagulation in the lower internal quadrant of the prefrontal region of the brain, during a period of 3 years is reported. Brief progress reports only are provided on 3 of the cases, which have been reported previously, but the remaining 9 are described in considerable detail. There were no operative deaths, but one patient developed epilepsy after the operation. Three patients have died since the operation, one from colonic perforation, one from paratyphoid infection, and one following emergency colectomy. The authors claim that in ulcerative colitis with severe haemorrhage it is possible by this method to avoid ileostomy or colectomy in most cases. [The follow-up was in no case sufficiently long to prove the value of prefrontal surgery in this notoriously variable disease.]
W. A. Bourne

Cardiovascular System

626. **The Syndrome of the Suspended Heart**
W. EVANS and H. G. LLOYD-THOMAS. *British Heart Journal* [*Brit. Heart J.*] **19**, 153–158, April, 1957. 4 figs., 10 refs.

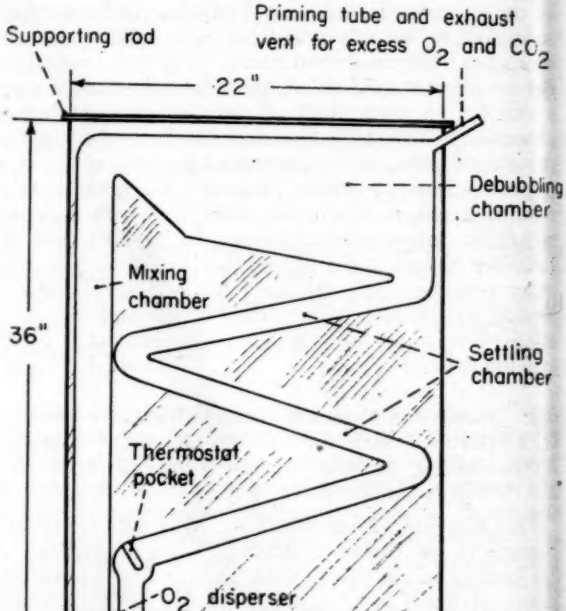
In 13 patients seen at the London Hospital an electrocardiographic pattern was noted which appeared to suggest the presence of myocardial ischaemia or hypertrophy. The T wave was inverted and/or the S–T segment was depressed in Leads III, III R (Lead III recorded in deep inspiration), II, and sometimes CR7. The R wave was low in Lead I and tall in Leads II and III. Tracings were taken in the reclining position, and when repeated after strenuous effort showed no change in the abnormality. None of the patients was hypertensive or receiving digitalis, and all appeared to have normal hearts. The majority were young adults of slender build.

On radiological examination the heart was seen to be of normal size. There was no emphysema. On deep inspiration the heart and diaphragm became unusually separated, revealing the inferior vena cava clearly in the oblique views. The authors consider that this separation of the inferior surface of the heart from the diaphragm, rendered particularly obvious on inspiration, accounts for the unusual electrocardiographic pattern, which is, of course, benign in nature. *J. A. Cosh*

627. **Measurement of Cardiac Output and Central Volume by a Modified Decholin Test of Circulation Time**
H. L. CONN, D. F. HEIMAN, and C. R. JOYNER. *Circulation* [*Circulation* (*N.Y.*)] **15**, 245–250, Feb., 1957. 1 fig., 4 refs.

628. **A Self-contained, Disposable Oxygenator of Plastic Sheet for Intracardiac Surgery. Experimental Development and Clinical Application**
V. L. GOTT, R. A. DEWALL, M. PANETH, M. N. ZUHDI, W. WEIRICH, R. L. VARCO, and C. W. LILLEHEI. *Thorax* [*Thorax*] **12**, 1–9, March, 1957. 4 figs., 5 refs.

The apparatus described in this paper has been evolved at the University of Minnesota Hospitals, Minneapolis, since 1955, during which time over 200 cardiac operations have been performed under direct vision, the circulation through the heart and lungs being totally by-passed. The apparatus consists of a vertical mixing tube, at the lower end of which are the blood and oxygen inlets, a debubbling chamber, and a settling chamber arranged in two limbs with a total length of about 5 feet (1·52 m.) (see figure). It is made by fusion of two sheets of polyvinyl plastic and will shortly be available commercially being supplied complete with antifoam in the debubbling chamber, sterile, and ready for use. It is suspended from a spring balance, which permits the maintenance of a constant blood volume in the unit, and is warmed by an external heater controlled by a thermostat placed in a pocket at the lower end of the settling chamber. Blood is pumped through the oxygenator by a "sigma-motor" or a rotating-cam pump at rates up to 3·5 litres a minute. Heparin is added to the donor blood used for priming the apparatus, and on completion of the perfusion protamine is given intravenously to the patient in dosage according to weight. Oxygen enters the mixing tube through a disperser consisting of a small cribriform plate.



During the development of the pump-oxygenator many animal experiments were carried out and numerous metabolic and biochemical observations made, the results of which are presented. The average oxygenation was 96%, the arterial *p*H remained normal, and there was very little haemolysis. The short debubbling tube proved completely efficient and there was no air embolism. The apparatus in its present form has been used for operations on 3 human patients for repair of ventricular septal defects; 2 are well, and the death of the third was not attributable to the oxygenator. *M. Meredith Brown*

629. **Dye-dilution Curves from Left Heart and Aorta for Localization of Left-to-right Shunts and Detection of Valvular Insufficiency**

E. BRAUNWALD, H. L. TANENBAUM, and A. G. MORROW. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **94**, 510–512, March, 1957. 3 figs., 6 refs.

A double hump in the dye dilution curve obtained by the intravenous injection of an indicator dye (azovan (Evans) blue or indigo carmine) and the subsequent determination of its concentration in the peripheral circulation may indicate the presence of a right-to-left shunt. The location of such a shunt, however, may be uncertain unless the dye is injected at a site near the defect—for example, into the left atrium or left ventricle by transbronchial puncture. Injection of the dye through an arterial catheter distal to an incompetent aortic valve is followed by a washing back and forth of the injected dye and a prolongation of the falling limb of the dye dilution curve. [No reference is made to the work of Korner and Shillingford, who originated this method of study of valve incompetence.] *J. McMichael*

630. **The Significance of Nonbacterial Thrombotic Endocarditis: an Autopsy and Clinical Study of 78 Cases**

R. A. MACDONALD and S. L. ROBBINS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 255–273, Feb., 1957. 3 figs., 13 refs.

In the opinion of the authors not enough importance is attached to the finding of non-bacterial thrombotic endocarditis at necropsy. Often referred to as terminal endocarditis, endocarditis simplex, or marantic endocarditis, it is considered by many to be a terminal condition and without clinical significance. In support of their view the authors describe 78 cases of the condition found during the course of 18,486 consecutive postmortem examinations over 22 years at the City Hospital, Boston, Massachusetts. Of the 78 cases, 40 were in men and 38 in women ranging in age from 18 to 90 years, 69 of the patients being over 49. The chief underlying diseases in these cases were cancer, heart failure, and vascular thromboses. The mitral valve was most commonly affected, and the condition had to be distinguished from the other common types of endocarditis—bacterial and rheumatic. Important for histological differentiation is the fibrocollagenous degeneration of the valve with a relative lack of cellular infiltration of the valve beneath the thrombus. An important clinical point that emerges from this study is that in 11 of the 78 cases there was evidence of multiple peripheral emboli which presumably came from the diseased valve. The authors suggest that such thrombus formation may be due to the patients entering a phase of their disease in which the blood becomes hypercoagulable. Their investigations ruled out the possibility that the lesions represented vegetations of bacterial endocarditis sterilized by previous antibiotic therapy.

The paper contains some excellent photomicrographs of the condition under low-power magnification, together with 2 illustrative case reports. *G. S. Crockett*

631. **Right-bundle-branch Block in Young Hospitalized Males. Report of Thirty-three Cases**

J. I. BRODY, L. H. GOLDEN, and J. L. TOBIN. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 250–253, Feb. 7, 1957. 11 refs.

An analysis of the electrocardiograms of 3,369 male patients aged 17 to 24 who had been admitted to United States Air Force hospitals revealed the presence of 289 (8·5%) that were considered abnormal. Among these were 33 cases of right bundle-branch block, that is, 11·4% of the abnormal tracings, or less than 1% of the total number in the series. Electrocardiographically, a diagnosis of complete block was made in 17 cases, in 10 of which there was electrocardiographic evidence of hypertrophy of the right ventricle. Of these 10 patients, 4 had clinical evidence of intrinsic heart disease, while the remaining 6 had no evidence of cardiovascular disease on physical examination, radiography, or fluoroscopy. Of the 7 patients with complete block without evidence of right ventricular hypertrophy, only one had any evidence of intrinsic heart disease. Of the 16 patients with incomplete right bundle-branch block, 3 had evidence of right ventricular hypertrophy, and all these 3 had evidence of intrinsic heart disease. Of the 13 with incomplete block without right ventricular hypertrophy, only 3 had evidence of intrinsic cardiovascular disease. Of the 22 patients with no evidence of cardiovascular disease, 6 had pneumonia and 5 some other type of infection.

It is concluded that " in young people the electrocardiographic discovery of right-bundle-branch block or hypertrophy of the right ventricle does not imply *a priori* cardiovascular or cardiopulmonary disease, if the remainder of the examination is negative ".

[A careful follow-up of a series such as this would provide much useful information.]

William A. R. Thomson

632. **The Volume of Distribution of High Molecular Weight Dextran and Its Relation to Plasma Volume in Man**

A. B. CRAIG and C. WATERHOUSE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **49**, 165–171, Feb., 1957. 2 figs., 26 refs.

In experiments carried out at the University of Rochester School of Medicine, New York, on 3 healthy subjects dextran of high molecular weight (average 194,900) was injected intravenously to give an initial concentration in the serum of about 70 mg. per 100 ml. The concentration fell exponentially by about 2% per hour during the 4 hours after injection. Arterio-venous difference was negligible 3 minutes after a rapid injection of the dextran solution into the right ventricle. The average volume of distribution of dextran (" dextran space ") was 41·0 ml. per kg. body weight in 11 normal resting men (coefficient of variation ±12%). It is concluded that this high-molecular-weight dextran is very suitable for the measurement of plasma volume, as it is evenly and quickly distributed in the plasma with minimal loss into the extravascular compartments.

Gerald R. Graham

o

633. **The Relative Volumes of Distribution of I^{121}-tagged Albumin and High Molecular Weight Dextran in Normal Subjects and Patients with Heart Disease**
J. R. JAENIKE, B. F. SCHREINER, and C. WATERHOUSE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **49**, 172–181, Feb., 1957. 1 fig., 21 refs.

In 10 normal subjects and 15 patients in heart failure with oedema plasma volume was measured by means of serum albumin labelled with radioactive iodine (^{131}I) and, simultaneously, by means of high-molecular-weight dextran [see Abstract 632]. The plasma volume as calculated from the concentration of radioactive albumin was significantly greater than the value calculated from that of dextran in all instances but one; it was greatest in the patients with heart disease. Successful treatment of cardiac failure with disappearance of oedema did not alter this difference. The data indicate that the radioactive albumin escapes into the extravascular compartments during the mixing period to a greater extent than dextran. Its use thus gives plasma volume values which are falsely high, especially in the presence of heart disease.

The results with high-molecular-weight dextran confirmed previous studies with other methods which showed an increased plasma volume in congestive heart failure. *Gerald R. Graham*

CONGENITAL HEART DISEASE

634. **Ebstein's Anomaly**
S. G. BLOUNT, M. C. MCCORD, and I. J. GELB. *Circulation* [*Circulation* (*N.Y.*)] **15**, 210–224, Feb., 1957. 11 figs., 33 refs.

To illustrate the characteristic clinical and other findings, 4 cases of Ebstein's anomaly are described in which the diagnosis was confirmed by cardiac catheterization. Two of the patients were acyanotic adults who had physical signs closely resembling those of acquired mitral or tricuspid valve disease; the authors suggest that because of this similarity, which has frequently been noted, a proportion of cases of Ebstein's disease in adults are probably erroneously diagnosed as cases of rheumatic valvular disease. The electrocardiographic and radiographic features which may be of value for diagnosis are discussed and the literature is extensively reviewed. The occurrence of paroxysmal tachycardia and other arrhythmias together with complete or incomplete right bundle-branch block is characteristic and has some diagnostic value. Enlargement of the right atrium as part of an enlarged, quiet heart with a globular silhouette, small aorta and pulmonary artery, and usually decreased vascularity of the lung fields is also characteristic. It is pointed out, however, that cardiac catheterization " continues to be the most effective means of confirming the presence of this anomaly ", the diagnostic features being enlargement of the right atrium, displacement of the tricuspid valve to the left, normal right ventricular, pulmonary arterial, and pulmonary arterial wedge pressure, and absence of an arterio-venous shunt. *James W. Brown*

635. **The Interpretation and Diagnostic Value of Oximetrically-recorded T-1824 Dye Curves in Congenital Heart Disease**
C. B. CHAPMAN, J. H. MITCHELL, J. F. GLOVER, and W. F. MILLER. *American Heart Journal* [*Amer. Heart J.*] **53**, 519–529, April, 1957. 8 figs., 9 refs.

The value of dye-dilution curves in the identification of the site and direction of an intracardiac shunt has been investigated at the University of Texas Southwestern Medical School, Dallas, 39 patients with congenital heart disease (including 20 children) being studied, of whom 12 had right-to-left, 11 had left-to-right, and 16 had mixed shunts, while 17 normal subjects and 8 patients with congestive cardiac failure served as controls. It was found that if at least 10 mg. of azovan blue (T-1824) was injected into the right atrium the dilution curves obtained directly by serial sampling from the femoral artery were comparable to those obtained indirectly by means of an ear oximeter in normal subjects. Oximetric dye-dilution curves were therefore obtained from the patients with congenital heart disease and the findings were correlated with the anatomical diagnoses made by estimation of oxygen saturation during cardiac catheterization.

In these patients the most valid indication of a right-to-left shunt was found to be a shortened " appearance time " (24 out of 28 cases), while the ratio " build-up time : appearance time " was increased in 19 out of 28 cases. A double-peaked curve did not always indicate a right-to-left shunt. Serial dilution curves from different injection sites within the heart or pulmonary artery enabled the site of the shunt to be correctly identified in 14 out of 26 cases of right-to-left shunt. No single abnormality of time interval or ratio indicated a left-to-right shunt, but the combination of normal " appearance time " and prolonged " disappearance time " was most suggestive.

The authors consider that if suitable apparatus is available the dye-dilution technique should be included as part of the routine procedure at cardiac catheterization, especially if there is reason to suspect the presence of right-to-left shunt. *D. Emslie-Smith*

636. **The Outlook for Children with Congenital Aortic Stenosis**
I. B. BRAVERMAN and S. GIBSON. *American Heart Journal* [*Amer. Heart J.*] **53**, 487–493, April, 1957. 13 refs.

Since few detailed accounts have appeared of the course and prognosis of congenital aortic stenosis in children, the authors have reviewed 85 such cases in patients under 16 years (67 boys and 18 girls) seen during the past 8 years at the Children's Memorial Hospital, Chicago. None had a history of rheumatism, all had the classic physical signs of aortic stenosis, 2 had associated patent ductus arteriosus, 3 had aortic coarctation, and one had fibrocystic disease.

An examination has been made or a report obtained on 73 of these patients since January, 1956, their ages ranging from 3 months to 19 years. Of these, 41 have no symptoms, 26 have symptoms, and 6 (8·2%) are dead. Of the children who died, 4 did so very suddenly and

3 had at least one syncopal attack before the fatal one; 2 tired easily and 2 had epistaxis; in 4 the heart was enlarged on radiography and in 3 there were electrocardiographic signs of left heart strain.

Of the 67 survivors, 44 can compete with their contemporaries, 14 cannot do so fully, and 9 cannot compete at all. Of the 26 patients with symptoms, 9 are easily fatigued, 6 have headaches, 4 become dizzy, 4 are dyspnoeic on exertion, 4 have epistaxis, and 3 have leg pains; in 5 of these children the heart is enlarged and in 10 there are cardiographic indications of left heart strain. Many of the 41 symptomless survivors are very active and several are athletes; 11 have large hearts and 14 have evidence of left heart strain.

The authors conclude that congenital aortic stenosis is not an innocent disease, and suggest that patients who are severely handicapped or have cardiac enlargement or electrocardiographic changes should be operated upon as soon as the procedure is proved to be relatively safe.

D. Emslie-Smith

637. **Clinical Experiences in the Surgical Treatment of 143 Patients with Patent Ductus Arteriosus**

H. E. MOZEN. *American Journal of Surgery* [*Amer. J. Surg.*] **93**, 361–366, March, 1957. 4 figs., 9 refs.

In this paper from the Western Reserve University School of Medicine and the University Hospitals, Cleveland, Ohio, the author reviews 143 cases of patent ductus arteriosus operated upon between 1940 and 1955, all of which have been followed up for at least 9 months. The series contained the usual preponderance of females (67·1%). No symptoms were recorded in 41·3%, the only complaint being the presence of a murmur. There was evidence of cardiac failure in 42·0%, and of asthenia and poor nutrition in 22·4%. The operation favoured is division and suture of the ductus, which was performed in the last 88 cases, rather than simple ligation. Postoperative deaths numbered only 3, and 2 of these occurred in patients with complicated ductus.

[This is a useful review of the condition, but the late follow-up is not sufficiently full to convey a picture of the end-results of operation.] *R. G. Rushworth*

638. **The Effect on the Left Ventricle of Surgical Closure of a Widely Patent Ductus Arteriosus.** (Retentissement ventriculaire gauche de la fermeture chirurgicale des canaux artériels à débit élevé)

P. SOULIÉ, J. MATHEY, J. NOUAILLE, O. SCHWEISGUTH, P. VERNANT, P. CORONE, and G. O. OUSTRIÈRES. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] 50, 97–103, Feb., 1957. 2 figs.

The steep increase in the resistance to left ventricular outflow after closure of a patent ductus arteriosus may account for changes in the T wave of the electrocardiogram (ECG) which sometimes follow this operation. In an infant of 7 months observed at the Hôpital des Enfants-Malades, Paris, closure of the duct was followed next day by severe left ventricular failure which was relieved only by direct aspiration of blood from the right ventricle. The ECG 24 hours later showed the pattern of left ventricular stress. A less dramatic episode of failure occurred one week later. In 2 children aged 11 and 13 years respectively the effects on the left ventricle of closure of the duct were less startling. One showed changes in the ECG on the 11th postoperative day; the other suffered tachycardia with systemic hypertension on the day following operation, and the ECG revealed the pattern of left ventricular stress; improvement quickly followed the administration of digitalis, a mercurial diuretic, and reserpine.

The authors observe that awareness of the possibility of such developments will enable appropriate measures to be taken (1) in prevention, by avoiding excessive replacement of blood loss, and (2) in treatment, by immediate cardiac aspiration if no suitable vessels are accessible. Moreover, they recommend the routine use of a low-salt diet, diuretics, and digitalis after operation for patent ductus arteriosus. Similar complications may follow the closure of any large left-to-right shunt and may partly account for the risk of operating on intraventricular defects in the presence of pulmonary hypertension. *R. S. Stevens*

CHRONIC VALVULAR DISEASE

639. **Percutaneous Left Ventricular Puncture in the Assessment of Aortic Stenosis**

P. FLEMING and R. GIBSON. *Thorax* [*Thorax*] **12**, 37–49, March, 1957. 10 figs., 25 refs.

In order to determine the value of percutaneous left ventricular puncture in the preoperative assessment of aortic stenosis, 28 pressure records so obtained at Guy's and Brompton Hospitals, London, have been analysed. All the patients concerned were considered to have aortic stenosis, and in 17 there was also clinical evidence of aortic regurgitation. Brachial arterial pressures were recorded either simultaneously or in immediate succession to the ventricular tracings, and in 17 instances cardiac output was measured by means of right heart catheterization. The left ventricular pressure pulse in aortic stenosis is described. An "a" wave due to left atrial systole is usually present in the end-diastolic portion. The systolic pressure is high (ranging from 140 to 325 mm. Hg in the present series) and the pulse wave is more sharply peaked than normal, both isometric contraction time and ventricular systolic upstroke time being abbreviated. Owing to lengthening of the phase of reduced ejection, however, the total ventricular ejection period is prolonged.

Aortic valvotomy was subsequently performed on 18 patients, and a surgical estimate of the degree of stenosis was available for 16 of these. Neither the peak systolic pressure gradient across the valve nor the prolongation of the ventricular ejection period (corrected for differences in cycle length) proved to correlate closely with severity of stenosis, presumably because these parameters are appreciably influenced by variations in stroke volume and hence by the presence and degree of regurgitation. Cardiac output was measured in 8 of the cases, and the relationship between systolic gradient, stroke volume, and ejection period was expressed by means of the

hydraulic formula of Gorlin and Gorlin in terms of aortic valve area. This calculated figure is not expected to agree precisely with the true area since in the presence of regurgitation measurement of output by the Fick principle underestimates the actual forward flow, while if stenosis is dominant the formula tends to overestimate valve size. Nevertheless, there was sufficient correlation to suggest that the calculated value may be of help in assessing doubtful cases. It is tentatively suggested that if it exceeds 1 sq. cm. and the degree of regurgitation is uncertain aortic stenosis is unlikely to be severe enough to warrant valvotomy.

Analysis of the brachial arterial pressure records confirmed the unreliability of the pulse pressure as an index of the degree of stenosis. The brachial systolic upstroke time, however, appears to be a more helpful measurement; this was invariably prolonged, and when related to the normal value for the pulse rate, correlated fairly well with the severity of the stenosis. *S. G. Owen*

640. **Epilepsy and Mitral Stenosis**

C. G. Baker and T. R. L. Finnegan. *British Heart Journal* [*Brit. Heart J.*] **19**, 159–163, April, 1957. 8 refs.

Of some 600 patients with mitral valve disease seen at Guy's Hospital, London, 22 (7 males and 15 females) had epileptiform convulsions. The average age of the patients was 34 years, and age at onset of the fits ranged from 19 to 47 years. Generally the fits began after the onset of symptoms of mitral disease. A family history of epilepsy was obtained in only one case. The fits were attributed to epilepsy in 2 cases only, in both of which the mitral disease was mild. In the remaining 20 cases fits were attributed to concurrent or previous cerebral embolism on the basis of incidence of auricular fibrillation, severity of associated mitral stenosis, relationship of fits to valvotomy, occurrence of hemiplegia or of other systemic embolism, and evidence of a focal cerebral lesion on electroencephalography. In the authors' view it is important to recognize that recurrent convulsions may follow focal cerebral damage due to previous cerebral embolism, and that anticonvulsant drugs are effective in the treatment of these cases. *J. A. Cosh*

641. **Arterial Embolism in Mitral Stenosis and Commissurotomy.** (Embolies artérielles du rétrécissement mitral et commissurotomie)

G. Ricordeau, B. Coblentz, and J. Lenègre. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **50**, 112–125, Feb., 1957. 21 refs.

To what extent does the postoperative diminution in the incidence of arterial embolism in cases of mitral stenosis treated by commissurotomy compensate for the increased operative risk, taking into account the prophylactic measures available during the intervention? To answer this question the authors have studied 370 cases of commissurotomy performed at the Hôpital Broussais, Paris, during the 5 years 1951–6. In all, 48 patients (12·9%), of whom 5 were males, had suffered previous systemic embolism, totalling 71 incidents. At operation 16 were in sinus rhythm and 32 in auricular fibrillation; auricular thrombus was found in 12 of the latter. Three of these 48 patients suffered embolism, which was fatal in 2 cases, at operation. Altogether there were 4 operative deaths in this group (8·3%) and 26 in the remaining 322 cases (8·1%). Death occurred subsequently in 3 more cases in the group with preoperative embolism, but none of the remaining 41 patients have suffered any recurrence of embolism.

The authors note that the over-all incidence of arterial embolism in their series is comparable to that reported in other series. They discuss the importance of cerebral location (usually over 50%), the increased risk with advancing age, and the danger of auricular fibrillation. Auricular thrombi were found three times more often in the cases with a previous history of embolism than in the remainder; nevertheless, no clot was found in the auricle in 36 of the 48. The authors suggest a preoperative course of anticoagulants (using heparin alone in the last 48 hours up to the midnight before operation) in all cases with auricular fibrillation, and they advocate protecting the cerebral arterial field in such cases with carotid clamps. Anticoagulants were used in all the cases in their series from about the 12th postoperative day for 2 months.

It is held that the absence of postoperative recurrence of embolism in 41 out of 48 cases with a preoperative history of embolism demonstrates the value of operation for such patients. *R. S. Stevens*

642. **Phonocardiographic Changes in Mitral Stenosis before and after Valvulotomy: a Correlation with Mitral Valve Size**

S. M. Steinzeig, S. T. Pinsky, M. M. Alimurung, and E. G. Dimond. *American Heart Journal* [*Amer. Heart J.*] **53**, 735–740, May, 1957. 4 figs., 9 refs.

643. **Effect of Mitral Commissurotomy on Coexisting Aortic-valve Lesions**

J. F. Uricchio and W. Likoff. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 199–204, Jan. 31, 1957. 7 figs., 4 refs.

In this paper are reported 3 cases admitted to Hahnemann Hospital, Philadelphia, in which mitral valvotomy was followed by aggravation of co-existing aortic valve lesions and death 20, 22, and 25 months later respectively. In such cases operative relief of the mitral stenosis increases the blood flow to the left ventricle and so increases the pressure gradient across the stenosed aortic valve. Left ventricular hypertrophy results, followed sooner or later by left-sided heart failure.

The importance of assessing the significance of coexistent aortic valve lesions is emphasized. The authors state that recently left-sided cardiac catheterization has been carried out in the theatre immediately before and after mitral valvotomy, and that a significant increase in the pressure gradient across the aortic valve after mitral valvotomy " is important evidence of dynamic aortic stenosis " and indicates the need for concomitant aortic valvotomy. " Unfortunately there is no satisfactory method of assessing the degree of aortic regurgitation." When serious aortic stenosis co-exists, the aortic valvotomy should be carried out first to allow for

the larger volume of blood reaching the left ventricle after mitral valvotomy. Technically, this is facilitated by using the right-sided approach to each valve, as described by Bailey *et al.* (*Surg. Clin. N. Amer.*, 1956, 36, 931). *F. J. Sambrook Gowar*

644. **Relation of the Postcommissurotomy Syndrome to the Rheumatic State**

D. L. Larson. *Circulation* [*Circulation (N.Y.)*] **15**, 203–209, Feb., 1957. 25 refs.

Reports show that 10% to 40% of patients subjected to mitral valvotomy for mitral stenosis develop the distressing condition known as " post-commissurotomy syndrome ". This occurred in 51 of 137 patients (out of 154) who survived mitral valvotomy at the Columbia–Presbyterian Medical Center, New York; in some of the cases there was a second attack. In no case was there circumstantial evidence of rheumatic activity such as the recovery of Group-A haemolytic streptococci from the throat or suggestive changes in antibody titre or the electrocardiogram. Further, the attacks were not prevented or influenced by salicylates, prednisone, or other drugs. A similar disorder has been observed following chest operations for a variety of unrelated conditions, and the author does not consider the syndrome to be due to an exacerbation of rheumatic activity. *James W. Brown*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

645. **The Hypocholesterolemic Effect of Phenylethylacetic Acid Amide in Hypercholesterolemic Atherosclerotic Patients**

B. Rossi and V. Rulli. *American Heart Journal* [*Amer. Heart J.*] **53**, 277–283, Feb., 1957. 1 fig., 9 refs.

A study is reported of the effect of phenylethylacetic acid amide on 14 patients, aged 39 to 70 years, in whom there was clinical, electrocardiographic, or radiological evidence of atherosclerosis. Dosage was 2 g. daily for 2 weeks and 3 g. daily thereafter, treatment being continued for 4 to 10 weeks (average 8 weeks).

The initial serum total cholesterol level varied from 204 to 378 mg. per 100 ml. (mean 249·4 mg. per 100 ml. in patients treated for 8 to 10 weeks and 278·2 mg. per 100 ml. in patients treated for 3 to 4 weeks). All the patients had been receiving, for some months or years previously, a diet which provided 500 to 600 mg. of cholesterol and 20 to 30 g. of fat daily; they were kept on the same diet during the period of study. At some stage of treatment in all except one of the patients there was a reduction in the plasma cholesterol level by well over 10% of the initial value. In patients treated for 8 to 10 weeks the reduction ranged from 5 to 71% (mean 43·3%). Generally, this effect was noted during the first week, but became much more marked when the dose was raised to 3 g. daily in the third week. It attained its maximum during the 10th week. The mean serum cholesterol level fell to normal (150 to 200 mg. per 100 ml.) for the major part of the treatment period and even fell below normal in the 10th week. One month after administration of the drug ceased the mean plasma cholesterol level was only 6·8% below the mean initial value. There were no side-effects from the drug, and no significant clinical improvement was observed. *Robert de Mowbray*

646. **The Epidemiology of Atherosclerosis among a Random Sample of Clothing Workers of Different Ethnic Origins in New York City. I. Prevalence of Atherosclerosis and Some Associated Characteristics**

F. H. Epstein, E. P. Boas, and R. Simpson. *Journal of Chronic Diseases* [*J. chron. Dis.*] **5**, 300–328, March, 1957. 4 figs., bibliography.

The investigation here reported was carried out at the Sidney Hillman Health Center, New York, on a random sample of about 1,000 persons belonging to a trade union whose 33,000 male and female members include nearly all workers making men's clothes in New York City. The sampling plan ensured a proportional representation of workshops and factories of different sizes and of the various trades within the union. The majority of the participants in the study came from unusually homogenous immigrant groups. About 90% of the men and 80% of the women were aged over 50, were born in Europe, and were of Jewish or Italian origin, but had lived for 40 years or more in the United States, so that while the groups adhered in many ways to their native customs and to their habitual pattern of life, they had become to some extent " Americanized ". Most of the Italians came from Southern Italy, and the Jews were predominantly of Eastern European origin. An additional group of family members, including 183 men and 272 women, were also examined.

Some interesting and somewhat surprising dietary data were collected in the course of these studies: it was found that the dietary fat intake was closely similar in both groups and made up approximately 35% of their total caloric intake; the proportion of fat of animal origin amounted to 80% among the Jews, while only 68% of the Italians' fat was of animal origin. The men and women of both ethnic groups were of relatively short stature and similar build and the mean relative weight (expressed in terms of deviation from "standard" weight) was similar in Italian and Jewish men (though the Italian women were appreciably heavier than the Jewish women), but showed no age trend in either sex or ethnic group. On the whole, however, the population studied was considerably overweight.

The over-all prevalence of coronary disease, adjusted to the age distribution of both groups, was 7·9% among 232 Italian men and 15·8% among 372 Jewish men. Differences existed between the two male groups with regard to the clinical manifestations of coronary disease: myocardial infarction and angina pectoris occurred with significantly greater frequency among the Jews, while coronary disease diagnosed on the basis of electrocardiographic evidence showed no appreciable ethnic difference. The prevalence of manifest coronary disease among women was lower than among men and was not appreciably different in the two ethnic groups, though wives in both groups showed a considerably higher pre-

valence than working women. The total prevalence of manifest heart disease of all types was 15·5% among Italian and 27·7% among Jewish men, and 18·7% and 11·3% respectively among the women.

The age-adjusted mean serum cholesterol levels were 222 and 241 mg. per 100 ml. for Italian and Jewish men, and 232 and 263 mg. per 100 ml. for Italian and Jewish women respectively. The values were significantly higher in women than in men regardless of ethnic group, and Jews had significantly higher values regardless of sex. In contrast to the serum cholesterol levels, the serum phospholipid levels were nearly identical in Jewish and Italian men, but Jewish women had significantly higher values than Italian women. The prevalence of calcification of the thoracic or abdominal aorta showed no ethnic difference. Systolic and diastolic blood pressure showed a rise with age, but again no ethnic difference. Neither could an ethnic difference be demonstrated in the prevalence of diabetes mellitus or in the serum uric acid level, though the latter was somewhat higher in men than in women.

A supplementary analysis of insurance statistics for the whole union membership also showed that both morbidity and mortality from coronary disease were greater among Jewish than Italian men living on disability or old age pensions, and that death from coronary heart disease was more common in Jewish than Italian men in employment. *Z. A. Leitner*

647. **The Epidemiology of Atherosclerosis among a Random Sample of Clothing Workers of Different Ethnic Origins in New York City. II. Associations between Manifest Atherosclerosis, Serum Lipid Levels, Blood Pressure, Overweight, and Some Other Variables**
F. H. Epstein, E. P. Boas, and R. Simpson. *Journal of Chronic Diseases* [*J. chron. Dis.*] **5**, 329–341, March, 1957. 2 figs., 25 refs.

A further analysis of data collected in the investigation described in the preceding paper [see Abstract 646] showed that the frequency of manifest coronary disease among Italian men increased in proportion with three variable factors—namely, serum cholesterol level, blood pressure, and body weight. While the over-all prevalence of coronary disease among Jewish men was much higher (15·8%) than among Italian men (7·9%), this difference was not due to the generally higher serum cholesterol levels among Jewish men since the frequency of manifest coronary disease was, in any case, higher among Jews quite independently of the serum cholesterol range. This lack of correlation between the predisposition of Jewish men for coronary disease and their tendency to have higher serum cholesterol levels is regarded as one of the most interesting findings in these studies. The population contained too few women with coronary disease for a similar analysis to be attempted. The presence of aortic calcification in *x*-ray studies was also more closely related in Italian men and women to the serum cholesterol level, blood pressure, and weight than in the Jews.

As the diets of the Jewish and Italian populations studied were closely similar, dietary factors could be largely excluded as an explanation of the difference in prevalence of coronary disease with the possible exception of the origin of fat in the diets concerned, 32% of the total fat intake in the Italian diet being of vegetable origin compared with only 20% in the Jewish diet. While admitting that some importance may be attached to this finding, the authors conclude that " undefined factors appear to be of considerable quantitative importance in determining the prevalence of coronary disease among certain predisposed groups and require further study, particularly by epidemiologic methods ".

[These two papers, together with others previously published by the same authors, are an important contribution to the epidemiology of atherosclerosis. They contain an extensive body of impressive evidence, the details of which cannot profitably be discussed in a short abstract.] *Z. A. Leitner*

648. **The Importance of Diet in the Treatment and Prophylaxis of Atherosclerosis.** (О значении диеты в лечении и профилактике атеросклероза)
F. K. Men'shikov and V. P. Sokolovskiĭ. *Советская Медицина* [*Sovetsk. Med.*] 18–23, No. 2, Feb., 1957.

In the treatment of diseases in the aetiology of which an alimentary factor plays a part, the use of dietary methods is essential. The significance of the alimentary factor, and in particular of the role of cholesterol, in the development of atherosclerosis has been confirmed experimentally by Anichkov and Khalatov. The effect of lecithin in delaying atherosclerosis in rabbits has been reported by Kanosch, Laschlo, and Perlzweig. Choline, like lecithin, has a marked lipotropic action and causes a fall in blood cholesterol level and a retrogression of atheromatous plaques in rabbits, as shown by Sinitsina, Steiner, Morrison, and Rossi.

In the dietary treatment of atherosclerosis, therefore, it is essential to increase the concentration of lecithin and lower that of cholesterol in the blood. While diet alone is not the sole source of blood cholesterol, and endocrine factors (such as the activity of the thyroid gland) must be taken into consideration, there is no doubt that diet plays an important part in determining the blood cholesterol content. A diet for the treatment of atherosclerosis must therefore fulfil the following conditions. (1) A minimum of animal fat (including egg-yolk) must be given, while the lecithin and choline content must be high. (2) The total caloric value must be reduced to the minimum compatible with the patient's activities. (3) Vitamins A and D, which tend to raise the blood cholesterol level, must be given sparingly, while Vitamins B, C, and P, which lower it, must be given in large quantities. (4) Plenty of cellular content must be included so that the excretion of cholesterol by the bowel is adequate. Such a diet should be given for about 6 weeks, the daily caloric content in the first week being 900 to 1,100 Cal., rising gradually to 2,000 to 2,200 Cal. in the last 2 weeks. Such a course can be repeated at varying intervals. Specimen menus are given.

This diet was successfully employed in 192 cases of atherosclerosis, with considerable relief of symptoms (such as anginal attacks, dyspnoea, and raised arterial

blood pressure). While the serum total cholesterol level was unchanged, there was a fall in the level of cholesterol esters, a rise in the lecithin: cholesterol ratio, a fall in the globulin content, and a rise in that of albumin. Blood viscosity and prothrombin index were reduced to normal in those cases in which they were high before treatment.

L. Firman-Edwards

649. **A Study of Myocardial Infarction in Women**
H. L. WEINREB, E. GERMAN, and B. ROSENBERG. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 285–300, Feb., 1957. 1 fig., bibliography.

Myocardial infarction is known to occur much more commonly in men than in women, and nearly all reports emphasize the importance of hypertension or diabetes in predisposing to this condition. In an attempt to throw light on the factors associated with coronary thrombosis in women the authors have carefully assessed the various features of 231 cases admitted to the Maimonides Hospital, Brooklyn, N.Y., over a period of 10 years. The patients were predominantly of Jewish descent, and their average age was 62. Diastolic hypertension (over 90 mm. Hg) was present in 51%, and 44% showed hypercholesterolaemia (over 280 mg. per 100 ml.). The incidence of diabetes mellitus was 53%. Angina which began at least a month before the first infarction occurred was noted in 47%. Only 2 patients survived more than 10 years, and 45 died in the first attack. Those with diabetes had the poorer prognosis. Two-thirds of the patients had a family history of diabetes, hypertension, or coronary arterial disease.

It is recommended that coronary thrombosis be seriously considered even in young women presenting a suggestive clinical picture, despite the absence of hypertension or diabetes. The role of female sex hormones as protective factors against atheroma is discussed, and it is suggested that a more extensive study of myocardial infarction in oophorectomized women would be of great interest.

G. S. Crockett

650. **Clinical and Anatomic Features in Five Hundred Patients with Fatal Acute Myocardial Infarction**
K. T. LEE, W. A. THOMAS, E. R. RABIN, and R. M. O'NEAL. *Circulation* [*Circulation* (*N.Y.*)] **15**, 197–202, Feb., 1957. 16 refs.

The clinical and anatomical features of 500 cases of acute myocardial infarction coming to necropsy at the Washington University School of Medicine, St. Louis, Missouri, during the period 1910–54 are described. In 429 of these cases it was possible to date the time of infarction. There was a preceding history of angina pectoris in half this number, and in the other half fatal myocardial infarction occurred without previous warning. Almost half the patients had evidence of old myocardial infarction in addition to a recent infarct, although only 25% gave a history of past infarction. Chest pain was present in 64% of the 429 patients. In 19% of the whole series with anatomical evidence of recent infarction a correct diagnosis was not made in life; this was in part due to the presence of complicating surgical operations or other conditions.

James W. Brown

651. **Distribution of Pain in Myocardial Infarction**
K. KREINES. *Circulation* [*Circulation* (*N.Y.*)] **15**, 348–352, March, 1957. 10 refs.

Studies of the embryology of the heart have suggested a difference in innervation of the right and left sides, with the possibility of pain patterns in myocardial infarction depending on the areas of heart muscle involved. To test this hypothesis the author examined the records of 104 patients dying from acute coronary occlusion or myocardial infarction on whom necropsy had been performed at Cincinnati General Hospital. In all cases the site of infarction could be accurately determined and a good history was available. Both walls were involved in 9 cases; of the remaining 95, 56 showed anterior- and 39 posterior-wall involvement. The infarction was considered to be massive if it involved the whole of the left ventricle, and such infarction was found in 29 cases in this series. Pain was either absent or minor in degree in 16 cases. There appeared to be a correlation between massive infarction and pain in the back and epigastrium; otherwise no significant association was observed between the site of infarction and the pattern of pain.

F. Starer

652. **Rupture of Papillary Muscles: Occurrence of Rupture of the Posterior Muscle in Posterior Myocardial Infarction**
R. J. SANDERS, K. T. NEUBUERGER, and A. RAVIN. *Diseases of the Chest* [*Dis. Chest*] **31**, 316–323, March, 1957. 15 refs.

The authors present clinical and necropsy details of 5 cases in which death occurred at the General Rose Memorial Hospital, Denver, Colorado, as the result of rupture of a papillary muscle complicating myocardial infarction. In 4 cases with posterior myocardial infarction the left posterior papillary muscle was ruptured. In the 5th case antero-lateral myocardial infarction was followed by rupture of both the anterior papillary muscle and the lateral wall of the left ventricle, a combination of complications not previously described.

Rupture of a papillary muscle usually occurs 3 to 17 days after the onset of symptoms of myocardial infarction shown electrocardiographically to be situated posteriorly. Clinically, there is a sudden onset of dyspnoea with signs of peripheral circulatory collapse and rapidly progressive pulmonary oedema. A harsh systolic apical murmur makes its appearance, or one previously present becomes accentuated, though sometimes it cannot be heard because of very loud respiratory noises. Death usually occurs from left ventricular failure with intractable pulmonary oedema. The prognosis is poor.

Only one case in the present series was diagnosed ante mortem, but the authors consider that it should be possible to differentiate rupture of a papillary muscle from acute cardiac dilatation and from rupture of the interventricular septum. In the latter event the systolic murmur is parasternal rather than apical, conduction defects are often present, and the electrocardiogram shows changes of anterior infarction.

Marcel Malden

653. **The Value of the C-reactive Protein Determination in Coronary Artery Disease**
M. C. Kozonis and I. Gurevin. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 79–85, Jan., 1957. 9 refs.

The authors have studied the response to the serum C-reactive protein test in 100 patients with unequivocal acute myocardial infarction, 50 with coronary insufficiency without infarction, 25 with the "coronary failure" syndrome, and 25 with a history and electrocardiographic (ECG) evidence of myocardial infarction 2 or more months previously. A commercially prepared antiserum giving a simple precipitation reaction was used for the test, which can be carried out in the consulting room. [For details, the original should be consulted.]

C-reactive protein appeared in the serum with Q-wave changes in the ECG in every case of acute myocardial infarction, although it was absent during the "premonitory phase" and before signs of myocardial necrosis were detected. It was consistently absent from the serum of patients with coronary insufficiency or coronary failure without myocardial infarction, and from the serum of patients with old, healed infarction. Persistence of C-reactive protein in high titre in the serum indicated a poor prognosis.

The C-reactive protein test is helpful in distinguishing cases of recent from old infarction and in the differential diagnosis of myocardial infarction and coronary insufficiency. In all these respects it is superior to the erythrocyte sedimentation rate. *Marcel Malden*

654. **Study of C-reactive Protein in the Sera of Patients with Acute Myocardial Infarction**
E. L. Levinger, H. Levy, and S. K. Elster. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 68–78, Jan., 1957. 3 figs., 18 refs.

The C-reactive protein test was carried out at the Mount Sinai Hospital, New York, on sera from 62 patients (44 males and 18 females), 50 of whom suffered from acute myocardial infarction and 12 from coronary insufficiency. The abnormal protein occurred in sera from 49 of the 50 cases of myocardial infarction and was absent from sera from all 12 cases of coronary insufficiency without myocardial necrosis. Serial estimations showed that the protein tended to persist for longer periods in the serum of patients in whom the original titre was highest, and that the amount of protein present correlated roughly with the other laboratory indices of myocardial infarction, such as fever, leucocytosis, and a raised erythrocyte sedimentation rate. In about 60% of patients C-reactive protein was present from the onset of myocardial infarction and disappeared within 1 to 2 weeks afterwards. In 4 patients, 2 of whom died, it persisted in the serum. In 2 other fatal cases (the total number of deaths was 5) C-reactive protein disappeared before death. It appeared in the serum before any changes were observed in the electrocardiogram in 15 cases, and after such changes were detected in 3.

The authors consider that the test is most useful for the early detection of myocardial infarction. They point out that a normal response with a single specimen of serum does not exclude a diagnosis of myocardial infarction, because in some cases the abnormal protein does not appear until 48 hours after the onset of pain. The C-reactive protein test cannot, however, be utilized to differentiate myocardial necrosis from other acute conditions such as pulmonary infarction or myocarditis, because the appearance of the protein in the blood is a non-specific indication of the occurrence of tissue trauma, necrosis, and inflammation. *Marcel Malden*

655. **Serum Glutamic–Oxalacetic Transaminase Activity in Conditions Associated with Myocardial Infarction. I. Bodily Trauma**
J. Lieberman, I. I. Lasky, S. I. Dulkin, and O. E. Lobstein. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 485–496, March, 1957. 4 figs., 21 refs.

The response of SGO-T [serum glutamic–oxalacetic transaminase] activity was studied in patients suffering bodily trauma, since such trauma may predispose to cardiac injury. Fifty-one patients involved in a variety of accidents were studied with electrocardiograms and serial SGO-T determinations. Although the majority (72·5%) were found to have elevated SGO-T levels, only 17·7% demonstrated additional evidence for cardiac injury; 47·1% revealed elevation of SGO-T activity apparently unrelated to cardiac injury or surgical procedures. It was concluded that SGO-T activity cannot be used as a specific test of cardiac injury in accident victims, since over 50% of the injured patients tested showed elevated SGO-T activity unrelated to demonstrable cardiac injury.—[Authors' summary.]

656. **Serum Glutamic–Oxalacetic Transaminase Activity in Conditions Associated with Myocardial Infarction. II. Cerebral Vascular Accidents and Congestive Heart Failure**
J. Lieberman, I. I. Lasky, S. I. Dulkin, and O. E. Lobstein. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 497–505, March, 1957. 2 figs., 8 refs.

The response of SGO-T activity was studied in conditions likely to be associated with myocardial infarction: cerebral vascular accidents and right heart failure. Of 21 patients with a diagnosis of recent cerebral vascular accident, 3 had underlying myocardial infarction, and 9 showed significant elevation of SGO-T activity with no evidence of cardiac involvement. SGO-T elevation occurred most frequently in cases of severe cerebral vascular accident, with curves resembling those of myocardial infarction except for a more gradual initial rise in activity. Hemorrhages and thromboses resulted in approximately equal elevations. It appears that the SGO-T activity determination is of limited value in the diagnosis of myocardial infarction when the picture suggests a severe, primary cerebral vascular accident.

In 11 out of 14 patients with moderate to severe right heart failure, there was no elevation of SGO-T activity, although 3 of these patients did demonstrate a gradual drop of over 15 units in their "normal" levels with the attainment of compensation. Three patients demonstrated definite SGO-T elevation which remained un-

explained. Right heart failure is only infrequently a complication of myocardial infarction. However, congestion of the liver may have to be considered in evaluating the SGO-T test when symptoms of myocardial infarction appear in patients already in congestive heart failure. Ordinarily, the presence of failure does not interfere with the interpretation of the SGO-T test in individuals with possible myocardial infarction.—[Authors' summary.]

657. **Limited Use of Anticoagulants in Acute Myocardial Infarction. Analysis of One Thousand "Good-risk" Cases**

H. I. Russek and B. L. Zohman. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 922–926, March 16, 1957. 18 refs.

The authors have studied the mortality and incidence of thrombo-embolic complications in 1,000 "good-risk" cases of acute myocardial infarction, as previously defined (*Circulation*, 1952, **5**, 707; *Abstracts of World Medicine*, 1952, **12**, 331), which were not treated with anticoagulants. The series consisted of two groups: (1) 489 cases selected and studied in retrospect; and (2) a further 511 cases selected for study at the time of their first examination. The basis of selection of both these groups as good-risk cases was the absence of previous infarction, severe or persistent shock, intractable pain, marked cardiac enlargement, gallop rhythm, congestive heart failure, auricular fibrillation or flutter, ventricular tachycardia, intraventricular block, or morbid state predisposing to thrombosis. All patients were treated conservatively with 3 to 4 weeks' bed rest and leg exercises from the onset.

In Group 1 the over-all mortality was 3·1%; mortality after the first 48 hours 1·7%; and incidence of thrombo-embolism 0·8%. In Group 2 the figures were 3·5%, 1·8%, and 3·7% respectively. Thrombo-embolic incidents in the latter group were all mild in degree, with no deaths, and no case of cerebral or peripheral arterial embolism occurred. In the combined series there were 33 fatal cases (3·3%), in only 9 of which anticoagulant treatment might have saved life (3 deaths from recurrent thrombosis, one from cerebral embolism, and 5 from unknown causes). Of the remainder, 16 deaths occurred unexpectedly during the first 48 hours, 4 were from non-cardiac causes, and 4 were from rupture of the left ventricle. Thus death from thrombo-embolic causes occurred in less than 1% of good-risk cases.

On the basis of these findings, and in view of the risk of haemorrhagic complications and of the adverse effect of the disturbance to the patient inseparable from treatment with anticoagulants in hospital, the authors consider that the use of these drugs is contraindicated in good-risk cases of acute myocardial infarction, though this conclusion does not detract from their established value in properly selected cases. *V. Reade*

658. **The Failure of Anticoagulant Therapy to Prevent Myocardial Infarction in Patients with Premonitory Symptoms of an Impending Coronary Occlusion**

M. Schlachman. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 728–735, April, 1957. 41 refs.

659. **Effect of Heparin on Lipemia-induced Angina Pectoris**

P. T. Kuo and C. R. Joyner. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 727–731, March 2, 1957. 5 figs., 18 refs.

The effect of heparin on acute anginal pain induced by administration of a fatty meal in patients with coronary arterial disease and old myocardial infarction was studied at the Hospital of the University of Pennsylvania, Philadelphia. A total of 15 attacks of angina were induced in 7 patients after a latent period of 5 to 5½ hours, and in all cases electrocardiograms, ballistocardiograms, and pneumograms were taken, the serum cholesterol and phospholipid levels were estimated, and the total esterified fatty acid and plasma turbidity values were determined; in addition serum lipoprotein patterns were obtained by paper electrophoresis. All these values were recorded before ingestion of the fatty meal (heavy cream), at the onset of anginal pain, and 15 minutes after an intravenous injection of either 2 to 5 ml. of saline solution or 5 to 25 mg. of heparin, the injection being given 15 minutes after the onset of pain. In 14 of the 15 attacks subjective relief was obtained 5 to 15 minutes after heparin administration, and this was confirmed objectively by improvement in the electrocardiogram, ballistocardiogram, and pneumogram. Similar but less permanent improvement was obtained with glyceryl trinitrate. Plasma turbidity and serum total fatty acid values rose sharply after the meal until heparin was given, and then fell suddenly. The serum lipoprotein pattern also showed considerable anodal migration after heparin. No such changes occurred when the pain was relieved by glyceryl trinitrate, and there were no changes in the serum cholesterol and phospholipid levels. No objective or subjective improvement followed intravenous injection of saline solution.

The authors conclude that post-prandial lipaemia can produce angina in susceptible patients and that efforts should be made to reduce it by restricting the dietary intake of fat with or without administration of an anti-lipaemic agent such as heparin.

J. Warwick Buckler

660. **Auxiliary Myocardial Vascularization by Prosthetic Graft Implantation**

S. Smith, M. Beasley, R. Hodes, H. Hall, E. Biel, and E. W. Huth. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **104**, 263–268, March, 1957. 6 figs., 3 refs.

The authors have attempted to augment the blood supply of the heart by grafting a homologous or "bank" blood vessel or nylon tube between the aorta and the myocardium. This procedure was carried out experimentally on 21 dogs and also performed upon 2 human subjects. The graft is anastomosed into the side of the aorta just below the arch with the aid of a Potts–Smith clamp and permitted to fill with blood. A series of nicks are made in the vessel to provide a number of points for the blood to extravasate into the myocardium; in the case of a nylon graft fine holes are made with an electrocautery. The graft is then tied to

a probe and drawn through the myocardium from below the coronary sulcus to the apex of the heart. The most avascular part of the heart is chosen, the probe being carried just below the epicardium but well within the muscle of the left ventricle. The clamp is removed, the end of the graft is trimmed flush with the myocardium, and the epicardium sutured over it. Pulsation in the vessel and a slowly growing but self-limiting haematoma indicate that the graft is functioning. The electrocardiogram immediately shows the characteristic changes of anterior infarction. Anastomosis between the grafted vessel and the coronary circulation was demonstrated in dogs 3 months or more after operation by post-mortem injection of the vessels.

The human subjects treated were: (1) a man of 43 years with anterior coronary insufficiency, whose internal saphenous vein was used as a transplant, with marked clinical improvement and return of the electrocardiogram to normal; and (2) a man of 50 years with marked antero-lateral ischaemia, in whom a nylon graft was used: his immediate progress was satisfactory and angina was relieved.

The authors are satisfied that an auxiliary circulation is created by this operation and that it does relieve the clinical and electrocardiographic manifestations of coronary insufficiency. *H. Sambrook Gowar*

661. **Surgical Treatment of Coronary Artery Disease: Medical Management and Evaluation of Results**
B. L. BROFMAN. *Diseases of the Chest* [*Dis. Chest*] **31**, 253–264, March, 1957. 5 figs., 5 refs.

Out of approximately 500 patients considered for the Beck-I operation for the treatment of coronary disease at the University Hospitals and Mount Sinai Hospital, Cleveland, Ohio, about 150 were rejected, 225 were operated upon, 12 died while awaiting operation, and about 110 refused operation. Patients operated upon varied in age from 27 to 72 years, and less than 10% were women; 75% had had at least one myocardial infarction, and 20% two or more. Angina pectoris was present in 95%. Duration of symptoms was from 4 months to 13 years. The operative mortality was less than 5%, but there were no operative deaths in the last 100 consecutive cases, even though 30 of them were "salvage cases".

Progressive improvement took place for a period of 1 to 6 months after the operation and almost all patients returned to work in 4 to 6 weeks. At long-term follow-up of the first 100 operated cases 15 were noted to have had severe "attacks", consisting in 3 of definite transmural infarction and in 12 of bouts of precordial pain. None of the 15 patients died and all returned to work. There was no improvement in 10 of the 100 cases. Electrocardiographic (ECG) evidence of myocardial regeneration did not occur and was not expected, but ECG evidence of further myocardial damage appeared only in 20%. Many patients, in parallel with clinical improvement, showed ECG evidence of improvement in the exercise tolerance test. In 3 of the patients there was clinical improvement but the electrocardiogram showed decreased exercise tolerance. Improvement in ballistocardiographic recordings was observed in 50% of the patients.

In the 6-month to 5-year follow-up of 137 consecutive cases, in which the expected mortality was calculated to be 30%, the actual mortality was 13·1%. Of the survivors, 45% were completely free from heart pain and 45% claimed marked improvement; 42% were able to work without limitation, and 48% were able to work with some limitation.

The author considers that the only indication for the operation is a positive diagnosis of coronary arterial disease, and he stresses that it should be performed early in the course of the disease, before extensive myocardial damage has occurred. In his view an early operation can reduce the 10 to 20% mortality associated with the first episode of myocardial infarction. The operation is contraindicated in acute myocardial infarction or when its impending occurrence is suspected, in younger patients with rapidly progressive symptoms, and in patients with severe hypertension or other associated serious disease. Cardiac enlargement and congestive failure are relative contraindications. Preoperatively all unnecessary investigations should be avoided. Patients with rapidly progressive disease or severe anxiety benefit from pre-treatment with antithyroid drugs. All patients should be fully digitalized. During the operation full oxygenation and maintenance of blood pressure are very important. When necessary, but not as a routine, procainamide or quinidine is used.

The author concludes that the effectiveness and the low mortality of Beck's operation justify its "early application to a majority of persons with coronary disease". *Marcel Malden*

BLOOD VESSELS

662. **Diagnosis of Arteriosclerotic Aneurysms of the Thoracic Aorta: Report of Six Cases**
I. STEINBERG. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 218–246, Feb., 1957. 8 figs., 30 refs.

The author prefaces this interesting paper from the New York Hospital–Cornell Medical Center by pointing out that, owing to the declining incidence of cardiovascular syphilis and the increase in longevity, arteriosclerosis as a cause of aneurysm of the thoracic aorta is becoming much more common than in the past. He describes the clinical features of 6 cases of thoracic aortic aneurysm due to such a cause seen during 1955–6, 3 of which were in men and 3 in women. The condition, he finds, occurs most commonly in the arch and descending portion of the aorta, rather than in the ascending portion and arch as in syphilis. Symptoms, as would be expected, are due to pressure on the nearby structures —recurrent laryngeal nerve, spinal column, and pulmonary artery. Despite the aortic involvement as seen radiologically, pulsatile movement of the aorta is generally absent. Hypertension is a usual accompaniment. The author considers that at present surgical treatment offers some prospects in carefully selected cases, though no firm views as to the likely prognosis can be formed

until a greater number of cases have been followed up. Of the 6 patients in the present series, 3 have died.

The paper contains some excellent angiograms.

G. S. Crockett

663. **Retrograde Perfusion of the Coronary Sinus for Direct Vision Aortic Surgery**

V. L. GOTT, J. L. GONZALEZ, M. N. ZUHDI, R. L. VARCO, and C. W. LILLEHEI. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **104**, 319–328, March, 1957. 2 figs., 18 refs.

Retrograde perfusion, via the coronary sinus, of oxygenated blood, in combination with a pump-oxygenator permits work on the open ascending aorta or coronary arteries for periods of up to 20 minutes in the dog. Flow studies of the coronary sinus venous drainage demonstrate in most instances a higher coronary flow in the by-passed heart even though the perfusion pressure in the aorta remains lower than for the non-by-passed heart. In 15 acute experiments the distribution (chamber-wise) of the retrograde perfusate has been studied. Also the coronary arteriovenous differences were determined for oxygen, glucose, and lactate. Twenty dogs were perfused seeking a survival experiment in each. Their hearts tolerated well 15 to 20 minutes of retrograde perfusion if the head of pressure was adjusted properly. The method of back perfusion via the coronary sinus has been tested in 7 clinical cases to date. In all instances the method appeared to protect the myocardium well against anoxia and coronary air embolism, permitting direct-vision reparative surgery for aortic stenosis and regurgitation, ruptured sinus of Valsalva, aortic–pulmonary septal defect, and complete transposition of the great vessels. The human heart responded well to this altered environment for periods up to 15 minutes.—[Authors' summary.]

664. **Dilatation of the Aorta Due to Granulomatous (Giant-cell) Aortitis**

J. V. O. REID. *British Heart Journal* [*Brit. Heart J.*] 19, 206–210, April, 1957. 3 figs., 19 refs.

665. **Treatment of Temporal Arteritis with Adrenal Corticosteroids. Results in Fifty-five Cases in which Lesion was Proved at Biopsy**

N. C. BIRKHEAD, H. P. WAGENER, and R. M. SHICK. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 821–827, March 9, 1957. 18 refs.

During the past 6 years at the Mayo Clinic 55 patients have been treated for temporal arteritis with adrenal corticosteroids. In reporting the results the authors stress that temporal arteritis is a self-limited and benign condition, with the important exception that it causes defective vision going on to blindness, in most cases due to ischaemic optic neuritis, and that the prevention of this grave complication should be the primary concern.

The 55 patients consisted of 28 men and 27 women, the oldest being 83 and the youngest 60 years of age. In 52 cases treatment was with cortisone and in 3 with prednisone. Cortisone was usually given intramuscularly in an initial dose of 300 mg. followed by 150 to 200 mg. a day, continued where possible for 6 weeks; prednisone in an intial dose of 75 mg. followed by 50 mg. daily for 6 weeks. Dosage of both drugs was then tapered off. There were no deaths, and in the majority of cases local and systemic symptoms were promptly relieved. Some loss of vision, considered to be part of the temporal arteritis syndrome, was noted in 36% of the cases on admission; 5 patients were blind in both eyes and 6 in one eye. Vision was not restored in any of these 16 eyes, but on the other hand bilateral blindness had not developed in any case at the end of treatment.

Difficulties in early diagnosis and in assessing which patients would be likely later to develop ocular manifestations led the authors to adopt the policy of treating all suspected cases of the disease with adrenal corticosteroids without waiting for biopsy if the latter procedure involved delay. They conclude that the adrenal corticosteroids are definitely indicated in the treatment of temporal arteritis, and that their chief value lies in controlling the disease so as to safeguard the remaining degree of vision. Their usefulness in bringing about histological healing is, however, still uncertain.

Joan Yell

SYSTEMIC CIRCULATORY DISORDERS

666. **Meprobamate as Adjuvant Therapy in Hypertension: a Preliminary Report**

R. A. DUNSMORE, L. D. DUNSMORE, A. F. BICKFORD, and A. GOLDMAN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 280–285, March, 1957. 28 refs.

Meprobamate was used as an adjuvant drug in the treatment of hypertension in 21 patients (20 negroes) at the General Hospital, Philadelphia. All except 2 of the patients were females, and their ages ranged from 28 to 60 years. The commonest symptoms were nervousness, headache, palpitations, weakness, insomnia, dizziness, and dyspnoea, in that order. In all the patients the diastolic pressure exceeded 110 mm. Hg, and 7 were classified as belonging to Group 4 (Smithwick), the numbers in Groups 1, 2, and 3 being respectively 2, 11, and 1. Meprobamate was given in a daily dosage of 1,600 mg., this being subsequently doubled in 3 cases and trebled in one case. After a period of observation varying from 1 to 5 months, during which the patients were seen at intervals of 1 to 2 weeks, symptomatic improvement was considered to be good in 10 patients, moderate in 6, and slight in 3; there was no such improvement in 2. Concurrently there was no fall in blood pressure in 12 patients, the remaining 9 showing falls in diastolic blood pressure ranging from 10 to 20 mm. Hg, which were considered inadequate.

The series included 9 patients previously treated with a preparation of *Rauwolfia serpentina* without any symptomatic improvement, who thus acted as their own controls, while in a comparable series of 20 patients given a similar preparation of *Rauwolfia serpentina* only 9 showed some improvement in symptoms. Side-effects of meprobamate were confined to anorexia in 4 patients

and constipation and fatigue in 2. The authors do not consider that meprobamate is a substitute for the specific antihypertensive drugs; indeed they gave pentolinium to those patients in whom the disease appeared to be progressive.

[A controlled comparative trial of meprobamate and some of the older drugs—for example, the barbiturates—in the relief of the symptoms of hypertension would be of interest.] *H. F. Reichenfeld*

667. **The Effect of Chlorisondamine on Renal Hemodynamics in Hypertensive Patients**
C. M. EBNER and Y. MORITA. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 424–429, April, 1957. 2 figs., 11 refs.

The effect on glomerular filtration rate and renal plasma flow of the intravenous administration of 2·5 to 10 mg. of chlorisondamine ("ecolid"), a quaternary ganglionic blocking agent, to 10 hypertensive patients was investigated at the City of Detroit Receiving Hospital (Wayne State University College of Medicine). The patients' beds were tilted 30 degrees from horizontal with the head up so as not to impede the pooling of blood in the dependent parts following the administration of the drug. Inulin and PAH clearances were determined before and one and 2 hours after injection of the drug, and the mean of the results for 3 10-minute periods recorded on each occasion.

All the patients showed a significant fall in mean arterial pressure. The mean glomerular filtration rate was reduced by an average of 32% of the control value at one hour and by 22% at 2 hours, the fall being consistent in all cases. The mean percentage change in renal plasma flow was within the standard error of the mean on both occasions and was therefore not significant, but the change in individual subjects varied considerably. Correlations were sought between the change in renal plasma flow and the fall in mean arterial blood pressure on the one hand and the change in renal vascular resistance on the other, and the dependence of renal plasma flow on renal vascular resistance was established.

Brief reference is made to the findings of other workers that both hexamethonium and pentolinium also cause a fall in glomerular filtration rate, and usually a reduction in renal plasma flow. *Gerald Sandler*

668. **Ambulant Treatment of Hypertension with Protoveratrine in Depot Form.** (Ambulante Hochdrucktherapie mit Protoveratrin in Depotform)
F. KAINDL, B. WATSCHINGER, and J. WUTTE. *Wiener Zeitschrift für innere Medizin und ihre Grenzgebiete* [*Wien. Z. inn. Med.*] **38**, 89–95, March, 1957. 6 refs.

Since the beginning of 1956 the authors have treated 50 ambulant patients with hypertension at the Second Medical Clinic of the University of Vienna with tablets containing 0·3 mg. of protoveratrine A (without protoveratrine B) in depot form ("PVA-retard"). The initial dose was half a tablet night and morning. This was increased according to the effect on the blood pressure to one tablet 3 times daily or more if necessary. The drug was well tolerated, and the maximum daily dose given was 1·8 mg. Side-effects, which occurred in 10% of all cases, were negligible and never serious enough to require discontinuance of treatment. They included transient occipital headaches, "flickering" of the eyes, feelings of heat, mild retrosternal pain, and nausea.

A study was made of 16 men and 13 women who were deemed to have carried out treatment satisfactorily, to have been adequately observed over an average period of 27 weeks, and to have had a sufficient number of controlled blood-pressure readings taken under constant conditions twice a week, the mean of several successive readings being recorded on each occasion. In this group PVA-retard treatment resulted in a statistically significant fall of the systolic pressure (below 200 mm. Hg) in 7 men and 7 women (48%) and of the diastolic pressure (below 110 mm. Hg) in 3 men and 3 women (21%). Although clinical amelioration or disappearance of hypertensive symptoms was a frequent finding, the subjective effect of the drug was not susceptible of statistical proof owing to the many imponderable associated factors. A combination of PVA-retard with other hypotensive drugs achieved success in a considerable number of patients with long-standing hypertension who had received no benefit from treatment with any one drug alone.

The authors point out that it cannot yet be determined whether the reduction of blood pressure by drugs either retards the progress of hypertensive disease or prevents the occurrence of its sequelae, and therefore whether the patients' expectation of life is increased. They regard the effect of PVA-retard as moderate only in respect of diastolic pressure, though the effect on the systolic pressure is gratifying. They consider the drug to be a valuable addition to the therapy of hypertension, either alone or in combination with other drugs, on account of its safety and ease of administration to ambulant patients. *E. S. Wyder*

669. **The Place of Adrenalectomy in the Treatment of Severe Arterial Hypertension**
C. C. WOLFERTH, W. T. FITTS, W. A. JEFFERS, and A. M. SELLERS. *Bulletin of the New York Academy of Medicine* [*Bull. N.Y. Acad. Med.*] **33**, 151–170, March, 1957. 13 refs.

During a recent 6½-year period at the Hospital of the University of Pennsylvania, Philadelphia, 168 patients suffering from essential hypertension were subjected to adrenalectomy, combined total or subtotal adrenalectomy and sympathectomy being carried out as a two-stage procedure in 155 and subtotal adrenalectomy only in the remaining 13. Maintenance therapy with cortisone was usually, but not always, required. Four patients survived subtotal adrenalectomy alone and were well 6 years later. Of 154 patients followed up for an average of 2½ years after combined total or subtotal adrenalectomy and sympathectomy, 114 survived, 25 of the 40 deaths occurring among 65 patients with hypertension of Group IV (Smithwick). Death was due to cerebrovascular disease in 18 cases, coronary arterial disease in 11, uraemia in 5, and other causes in 6; only one of these deaths occurred more than one year after

operation. There were no deaths due to congestive heart failure. A permanent fall in blood pressure occurred after operation in about three-quarters of the patients, and in about half the blood pressure became about normal. Cardiac function, optic-fundus appearances, and symptoms also improved, but renal function was unchanged. The adrenal glands removed appeared normal. Total and subtotal adrenalectomy were equally effective combined with sympathectomy.

The authors state that it is not possible to predict which patients will respond favourably to the combined operation. In their view such operation should be confined to those patients in whom it is necessary urgently to control the hypertension and who respond poorly to, or are unable to tolerate, antihypertensive drugs.

Bernard Isaacs

670. **Results of Nephrectomy in Hypertensive Patients**
G. J. THOMPSON. *Journal of Urology* [*J. Urol.* (*Baltimore*)] 77, 358–363, March, 1957. 11 refs.

At the Mayo Clinic approximately 3,000 patients were subjected to unilateral nephrectomy during the 15-year period 1940–54, and of these, 344 (11%) were found to have hypertension. For various reasons [not stated] 7 patients were excluded from the present study. Of the remaining 337 (194 females and 143 males), 39 had renal tumours, 119 an atrophied or hypoplastic kidney, while 179 suffered from miscellaneous renal conditions. A " good early effect " of nephrectomy was defined as a reduction in blood pressure to 140/90 mm. Hg, which was maintained when the patient was discharged from hospital. A " good late result " was recorded when the blood pressure remained below 140/90 mm. Hg for more than one year.

Of the 39 patients with renal tumours, 34 had hypernephroma, 4 epithelioma of the renal pelvis, and one had an encapsulated neurofibroma. A good early result was achieved in 12 of these patients, but a year later only 5 had a normal blood pressure.

Sympathectomy was performed in addition to nephrectomy in 29 cases in the series—19 of atrophic pyelonephritis and 10 of other forms of unilateral renal disease.

When these 29 cases and 39 of renal tumour were excluded there remained 100 cases of atrophic pyelonephritis and 169 cases of other renal conditions for analysis of the results of nephrectomy in cases of hypertension. It was found that the results were better after nephrectomy in patients with atrophic pyelonephritis than in those with other forms of unilateral renal disease, a good early effect being obtained in 63 out of the 100 in the former group, compared with only 64 (37·8%) in the latter group. After a follow-up period of one year or more the results were good in 35 (54·6%) of 64 patients suffering from atrophic pyelonephritis who were traced and in 25 of 100 with other renal conditions. Of the patients with atrophic pyelonephritis, 70% were females; 80% of them were under 50, whereas only 48% of those with other renal conditions were under this age.

Careful pathological examination did not reveal any definite histological lesions in the kidneys which could be compared with those in the kidneys of patients without hypertension. Neither the type nor the degree of pathological change influenced the outcome of operation, the removal of an uninfected hypoplastic kidney sometimes giving excellent results. Renal damage, except in cases in which hypoplasia was present, was extensive.

The author concludes that nephrectomy should be performed on hypertensive patients suffering from severe unilateral renal disease, provided there are no other conditions which contraindicate operation.

L. G. Fallows

671. **Clinical Studies on a Vasopressor Agent: Metaraminol (Aramine). III. Observations on Its Oral Use in the Treatment of Hypotension**
M. H. WEIL. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] 233, 367–374, April, 1957. 4 figs., 9 refs.

Observations on the effects of the oral administration of the vasopressor drug " metaraminol " (" aramine ") on 16 normotensive control subjects and 35 patients with symptomatic hypotension are reported from the University of Minnesota Hospitals, Minneapolis. Metaraminol is closely related chemically to ephedrine and amphetamine.

In 8 out of 10 normotensive subjects a prolonged pressor effect proportional to the dose occurred with doses of 30 to 45 mg., the onset being 45 minutes after the dose and the duration of effect up to 3 hours. Reflex vagal bradycardia occurred in 9 subjects, and significant toxic side-effects in one subject in whom a dose of 45 mg. produced an excessive pressor response.

The hypotensive group consisted of 26 men and 9 women, average age 64 years, who were suffering from systemic infection, neurological disorders, or myocardial infarction or had undergone surgical procedures. In 25 cases metaraminol had previously been given parenterally with good effect, and in these the effective oral dose was 5 to 6 times the parenteral dose. Of the whole group, a prompt and prolonged pressor response with control of hypotensive symptoms was obtained in 32 cases (91%) with an average oral dose of 25 mg. at intervals of 1½ hours, treatment continuing for an average of 8·5 days. Of the 8 patients with chronic idiopathic or neurological postural hypotension, 2 died while under treatment, one has been satisfactorily maintained on oral administration for 10 months, in 2 treatment was abandoned because of gastro-intestinal side-effects, and in 3 no further medication was considered necessary. Gastro-intestinal side-effects occurred in 7 cases altogether, and were more frequent in patients with chronic than with transient hypotension. Sinus bradycardia did not occur.

The author concludes that a dose of 10 to 75 mg. of metaraminol by mouth every 1 to 3 hours is safe and effective in the treatment of symptomatic hypotension due to systemic infections, myocardial infarction, or prolonged bed rest or after surgical procedures, but that the value of the drug and the dangers involved in its prolonged use in chronic idiopathic or neurological hypotension require further investigation.

Gerald Sandler

Haematology

672. **On Plasma Fibrinolytic Activity in Cryptogenetic Splenomegaly**
H. C. KWAAN, A. J. S. MCFADZEAN, and J. COOK. *Scottish Medical Journal* [*Scot. med. J.*] **2**, 137–150, April, 1957. 1 fig., 31 refs.

Cryptogenic splenomegaly, a disease which is observed among the Chinese and is often but not always associated with cirrhosis of the liver, was found to lead to spontaneous fibrinolytic activity of the plasma. In the study here reported from the Queen Mary Hospital, Hong Kong, in an attempt to determine the origin of this fibrinolytic activity, a number of tests were carried out on patients with cryptogenic splenomegaly before and after splenectomy. The well-known fibrinolytic response to trauma, operations, and adrenaline injections was much greater in the splenomegalic group than in controls, particularly in those with cirrhosis of the liver, but after splenectomy these responses were minimized, and the basal fibrinolytic activity approached normal levels. Plasma from blood obtained from the hepatic vein was less fibrinolytic than arterial or peripheral venous blood, and blood from the splenic vein was also inactive. It is therefore concluded that both the liver and the spleen have anti-fibrinolytic activity.

Attacks of diarrhoea and of gastro-intestinal haemorrhage appeared to cause an increase in fibrinolysis, whereas some time after operation and haemorrhage and during an attack of fever, fibrinolysis was inhibited. Portal vein thrombosis and carcinoma of the liver also reduced fibrinolysis, a finding which is the basis of useful diagnostic tests. In nearly all circumstances any increase in fibrinolytic activity was inhibited by administration of corticotrophin (ACTH) or cortisone.

The authors attempt to explain these findings, but admit that the mechanism of spontaneous fibrinolytic activity is very complex. [The original paper must be consulted by those interested in this subject.]

John Naish

ANAEMIA

673. **A Study of the Survival Rate of Cases of Sickle-cell Anaemia**
G. F. JACOB. *British Medical Journal* [*Brit. med. J.*] **1**, 738–739, March 30, 1957. 9 refs.

For a study of the survival rate in sickle-cell anaemia 3,362 samples of blood from adults of the Baganda tribe in Uganda were examined, sickling being found in 545 (16·2%), and were then subjected to paper electrophoresis. In 3 cases, which are described in full, the pattern of sickle-cell anaemia was observed. The author states that although proof of inheritance was lacking, the diagnosis of sickle-cell anaemia was considered to be established by the fact that other abnormal haemoglobins and also thalassaemia, which produce an electrophoretic pattern similar to that of sickle-cell anaemia, have not been observed in East Africa. Since the sickling rate was 16·2%, it was calculated that the finding of sickle-cell anaemia in 3 adults indicated a 14% survival to adult life. This, it is suggested, is one explanation of the continued presence of the sickling gene in the population. The estimates of some other workers, however, differ from these, and it is considered likely that the survival rate may vary in different parts of Africa, the variation being due probably to environmental factors, of which the prevalence of and mortality from malaria is but one.

J. L. Markson

674. **Erythroblastopenia with Giant Proerythroblasts in Kwashiorkor**
KHO LIEN-KENG. *Blood* [*Blood*] **12**, 171–182, Feb., 1957. 9 figs., 25 refs.

Among 92 children admitted to the Paediatric Clinic of the University of Indonesia, Djakarta, with severe malnutrition during the past 3 years were 7 cases of typical kwashiorkor in children aged 1½ to 8 years associated with a severe aplastic type of anaemia as evidenced by the peripheral blood picture and marrow puncture. In addition, in all these cases giant proerythroblasts or their precursors were found in the bone marrow; these cells varied in number from 0·6 to 4 per 1,000 nucleated bone-marrow cells. Irrespective of treatment the bone-marrow picture became normal in 3 cases and there was improvement in the peripheral blood associated with a reticulocyte crisis. Three of the children died in the aplastic phase.

The author compares the haematological picture in these cases to the acute aplastic crisis followed by remission that Owren first described in congenital haemolytic anaemia, and concludes that infection may play the same part as a trigger mechanism.

Janet Vaughan

675. **The Stomach in Hypochromic Anaemia**
J. BADENOCH, J. R. EVANS, and W. C. D. RICHARDS. *British Journal of Haematology* [*Brit. J. Haemat.*] **3**, 175–185, April, 1957. 12 figs., 13 refs.

Histological examination of specimens of mucosa obtained through a flexible gastric biopsy tube from the body of the stomach in 50 cases of hypochromic anaemia at the Radcliffe Infirmary, Oxford, revealed that the mucosa was normal or nearly normal in 7, gastritis with slight or moderate tubular damage was present in 23, gastritis with severe glandular atrophy in 18, and gastric atrophy in 2. In 8 control non-anaemic subjects normal gastric mucosa was obtained. Specimens taken in one case before and after treatment with iron showed that an improvement in the state of the gastric mucosa had occurred. Achlorhydria was twice as common in the anaemic patients as in 146 non-anaemic subjects, and in those under the age of 50 it was four times as common. There was a good correlation between the severity of the mucosal changes and the incidence of histamine-fast

achlorhydria, and a reduction in the secretion of pepsin and excretion of uropepsin. In some of the patients the secretion of intrinsic factor was impaired.

The evidence thus obtained suggests that the changes which occur in the mucosa of the stomach in hypochromic anaemia are the result rather than the cause of iron deficiency. *A. Ackroyd*

676. **Oral Maintenance Treatment of Pernicious Anaemia**
J. F. ADAMS. *Scottish Medical Journal* [*Scot. med. J.*] 2, 151–153, April, 1957. 12 refs.

The results obtained with preparations of cyanocobalamin (vitamin B_{12}) and intrinsic factor in the maintenance therapy of pernicious anaemia are reported in this paper from the Royal Infirmary, Glasgow. The diagnosis of pernicious anaemia was based on the presence of a megaloblastic bone marrow and histamine-fast achlorhydria, and the preparation used, which was in tablet form, contained 7·5 μg. of cyanocobalamin and 1·5 μg. of hog-stomach mucosa. Of the 73 patients included in the trial, 58 had been maintained previously on cyanocobalamin given parenterally and 15 had pernicious anaemia in relapse. All were seen every 4 weeks, and at least every 12 weeks the erythrocyte count, the packed-cell volume, and the haemoglobin value were determined. The serum level of cyanocobalamin was estimated by the method of Ross, 12 and 6 months before the end of the trial.

Only 38 of the patients were maintained in a satisfactory condition; in 11 there was a fall in the erythrocyte count to 3,000,000 per c.mm. or less, in 9 there were other clinical signs of cyanocobalamin deficiency, while in 15 the serum level of the drug was less than 100 $\mu\mu$g. per ml. The majority of patients were taking one tablet only each day (in order to achieve regular medication), but 5 of those in whom the erythrocyte count fell below 3,000,000 per c.mm. were refractory to 5 tablets daily and 2 others were refractory to 4 tablets daily. Of 3 patients maintained on 2 tablets a day 2 relapsed. The duration of the trial was determined in individual cases by a fall in the erythrocyte count below 3,000,000 per c.mm., when it was terminated.

The author concludes that oral preparations of cyanocobalamin with intrinsic factor are unsuitable for the maintenance therapy of pernicious anaemia.

John Naish

HAEMORRHAGIC DISEASES

677. **A Study of Hemophilia**
M. C. HARMON, A. ZIPURSKY, and M. E. LAHEY. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] 93, 375–384, April, 1957. 1 fig., 27 refs.

The nature of the disorder of blood coagulation in 32 patients who had been admitted to Cincinnati Children's Hospital during the period 1940–55 with the diagnosis of haemophilia was reassessed, particularly by means of the thromboplastin generation test (using barium sulphate instead of alumina for adsorption) and the method of "differential mixtures", in which the ability of plasma and serum known to be deficient in various factors to correct the patient's coagulation defect is determined. The thromboplastin generation test enabled a clear-cut division into 2 groups to be made with one possible exception. In 9 cases (28%) the patient's serum, when added to an otherwise normal system, failed to generate thromboplastin normally (1 to 35%), whereas normal values (73 to more than 100%) were obtained when the patient's plasma, adsorbed with barium sulphate, was used. This group was therefore deficient in plasma thromboplastin component (P.T.C.). In the remaining 23 cases (72%) abnormal values (3 to 60%) were obtained in the thromboplastin generation test with the patient's plasma treated with barium sulphate, whereas in 22 of the 23 cases normal results (>70%) were obtained with the patient's serum, and in one a borderline result of 70%. However, since confirmatory results were obtained in this last case in all the other tests used, all 23 cases in this group were regarded as deficient in anti-haemophilic globulin (A.H.G.). The "differential mixtures" test on the other hand was diagnostically unreliable, only 4 cases with P.T.C. deficiency and 9 with A.H.G. deficiency giving the expected "typical patterns". It is suggested that this may have been due to (1) difficulty in reading results when the patient's prothrombin consumption was near to normal, (2) use of test plasma from patients in whom the A.H.G. and P.T.C. deficiencies were only mild, and (3) incomplete removal of P.T.C. from the patients' plasma owing to the use of insufficient barium sulphate. Plasma prothrombin activity (measured by Quick's method) was normal in 29 cases, but in 3 (all A.H.G.-deficient) it was decreased. The cause of this could not be explained in one of the cases. In the other 2 cases (in brothers) normal values were obtained when bovine Ac globulin was added, and their plasma prothrombin content was also normal on assay by the TAMe method. They were therefore thought to have concomitant A.H.G. and Ac-globulin deficiency. The coagulation time (Lee-White) was normal (6 to 14 minutes) in 3 cases of P.T.C. deficiency and in 6 of A.H.G. deficiency. The serum prothrombin time (Stefanini) was normal in one case of P.T.C. deficiency and in 2 with A.H.G. deficiency. In 3 of the A.H.G.-deficient cases the serum prothrombin time could not be corrected by any of the "differential mixtures", and a circulating anticoagulant or inhibitor was thought to be present.

Clinically, there were no features peculiar to either A.H.G. or P.T.C. deficiency, nor was there any consistent relation between the clinical severity of the cases and the degree of abnormality of the laboratory tests.

M. Kendal

678. **A Concentrate of Human Antihaemophilic Factor. Its Use in Six Cases of Haemophilia**
R. A. KEKWICK and P. WOLF. *Lancet* [*Lancet*] 1, 647–650, March 30, 1957. 8 refs.

A concentrate of human antihaemophilic factor for the treatment of haemophiliacs has been prepared at the Lister Institute of Preventive Medicine, London. Preparation consists in rapid cooling of fresh citrated blood and centrifugation at 0° C. within 3 hours of withdrawal.

Water is added to the plasma and then, at −0·5° C., cold ethyl ether. The mixture is allowed to stand overnight at 0° C. Removal of the clear supernatant allows the residuum to be mixed and centrifuged. The packed precipitate is suspended in a sodium chloride–sodium citrate solution and the whole is centrifuged after addition of ethyl ether. The washing process proceeds again, and the final material is dissolved in the chloride–citrate solution to give a colourless and slightly opalescent solution which is frozen in 100-ml. amounts to −20° C. in containers for freeze-drying. All the procedures were carried out under aseptic conditions, thus ensuring the sterility of the product without the need for any active process of sterilization.

On the basis of assay *in vitro* the antihaemophilic activity in the final product has been consistently not less than 85% of the original material. The product was used in the management of 6 haemophiliacs, some with spontaneous bleeding, and some subjected to surgery, minor or major. The results were very satisfactory. It is pointed out that with this preparation the dangers of circulatory overloading are largely avoided, 100 ml. of the concentrate being equivalent to 1,000 ml. of fresh plasma.

A. Brown

679. **Blood Coagulation Defects in Kwashiorkor and Infantile Gastroenteritis**

C. MERSKEY and J. D. L. HANSEN. *British Journal of Haematology* [*Brit. J. Haemat.*] **3**, 39–49, Jan., 1957. 5 figs., 30 refs.

The haemostatic mechanism was studied in 58 children with kwashiorkor and 9 with gastroenteritis at the University and Groote Schuur Hospital, Cape Town. Among the 58 cases of kwashiorkor were 9 of purpura, but in only 3 of these was the platelet count below 100,000 per c.mm. None of the patients with gastroenteritis had purpura.

The majority of the patients studied had a prolongation of the one-stage clotting time. This was found to be due to a deficiency of Factor VII and to a lesser extent of prothrombin. There was a defective serum reaction in the thromboplastin generation test. Since the Christmas-factor content was normal, the authors suggest the possibility of a Factor-X deficiency. There was no deficiency of Factor V or of antihaemophilic globulin. The plasma defect was the same in kwashiorkor and gastroenteritis. These plasma clotting defects responded to the administration of a suitable diet; vitamin K appeared to be an important factor in the improvement.

A. S. Douglas

680. **The Bleeding Tendency in Chronic Renal Failure.** [In English]

B. B. KUHLBÄCK. *Acta medica Scandinavica* [*Acta med. scand.*] **157**, 173–177, April 18, 1957. 28 refs.

Investigations into the haemostatic mechanism in 30 patients with chronic renal failure are described from the Maria Hospital, University of Helsingfors. The majority of these patients were suffering from chronic glomerulonephritis or chronic pyelonephritis. In 4 of them there was clinical evidence of haemorrhage. Assessment of the haemostatic mechanism was by tourniquet test, whole-blood coagulation time, bleeding time, platelet count, and estimation of prothrombin concentration and serum calcium level. The tourniquet test gave positive results in nearly two-thirds of the cases. The platelet count was slightly reduced in 23 patients. The calcium concentration was often low.

The author suggests that the haemorrhagic state in uraemia may be vascular in origin.

A. S. Douglas

NEOPLASTIC DISEASES

681. **The Neurologic Manifestations of the Acute Leukemias: a Clinical Study**

C. E. WELLS and R. T. SILVER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 439–449, March, 1957. 12 refs.

In a series of 63 patients with proved acute leukaemia admitted to the National Cancer Institute, Bethesda, Maryland, over a period of nearly 3 years the incidence of neurological manifestations was relatively high, 22 out of the 42 who had died by the end of the period having had 27 such episodes, and neurological complications having occurred in 2 of the remaining cases. The majority were due to intracranial haemorrhage, but peripheral nerve involvement occurred in 3 patients.

A. Piney

682. **The Problem of Leukemia in Polycythemia Vera**

S. P. MASOUREDIS and J. H. LAWRENCE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 268–274, March, 1957. 2 figs., 18 refs.

In this report from the University of California the clinical and follow-up records of 22 patients with polycythaemia vera who eventually developed a leukaemic type of blood picture (Group I) are compared with those of 157 patients who did not (Group II). (In some of the Group-I patients the picture was that of myeloid metaplasia rather than of true myelogenous leukaemia.) The two groups were comparable in respect of age, sex, and duration of symptoms before treatment. The patients in Group I showed a significantly higher incidence of leucocytosis, thrombocytosis, and immature leucocytes in the peripheral blood before treatment with radioactive phosphorus (^{32}P) was started. The median survival after starting ^{32}P therapy was 13·3 years in Group II and 6·7 years in Group I. The authors conclude that the development of leukaemia in patients with polycythaemia vera is not directly related to ^{32}P therapy, and this excellent form of treatment should not be withheld on account of a risk which seems to be merely hypothetical.

P. C. Reynell

683. **Myleran Treatment in Chronic Granulocytic Leukaemia**

D. TURESSON. *British Journal of Haematology* [*Brit. J. Haemat.*] **3**, 220–226, April, 1957. 4 figs., 7 refs.

The author reports the results of treatment with " myleran " (1:4-dimethanesulphonyloxybutane; busulphan) in 39 cases of chronic granulocytic leukaemia at

the Jubilee Clinic, Göteborg, Sweden. Most of the patients were treated as out-patients, and the majority have been able either to continue working or to resume work in 4 to 8 weeks. All except those with an immature (mainly myeloblastic) blood picture have responded well, initial doses of myleran of 0·06 mg. per kg. body weight bringing the leucocyte count to normal levels within 2 to 8 weeks and the erythrocyte count and haemoglobin value to normal levels in a further 2 to 4 weeks. Maintenance doses ranging from 2 mg. per week to 4 mg. per day were then given thereafter. Remissions lasting up to 36 months have been obtained, but resistance to myleran has developed in some patients and 19 have died. The average duration of the disease has been 27·5 months, compared with 26·5 months in 28 patients treated by radiotherapy before myleran treatment was introduced. Severe toxic side-effects have been observed in only 2 patients, who developed thrombocytopenia. *A. Ackroyd*

684. **Desacetylmethylcolchicine in the Treatment of Myeloid Leukaemia**
A. M. JELLIFFE and J. E. MACIVER. *British Journal of Cancer* [*Brit. J. Cancer*] **10**, 634–641, Dec., 1956 [received April, 1957]. 3 figs., 5 refs.

The authors present the case histories of 4 patients who were treated at the Middlesex Hospital, London, with "colcemid" (methyldeacetylcolchicine). The first, a woman of 58 suffering from chronic myeloid leukaemia, responded for 2 years to splenic irradiation but with diminishing remissions. Further treatment with blood transfusions, cortisone, 6-mercaptopurine, and colcemid failed to produce a response and the patient died. The second patient, a 60-year-old man who had been treated for polycythaemia with deep *x* rays and radioactive phosphorus (^{32}P) for 8 years, presented a total leucocyte count of 146,000 per c.mm. and a haemoglobin level of 60%. Treatment with 5 mg. of colcemid daily for 12 days markedly reduced the leucocyte count, but with reduction of the dose to 3 mg. daily the count rose again rapidly. The patient died of hypostatic pneumonia before any further observations could be made. The third patient, a woman of 30, had suffered from chronic myeloid leukaemia for over 3 years. She responded to deep *x*-ray therapy, but with shortening remissions. Treatment with colcemid in doses up to 13 mg. daily was without effect. A satisfactory remission occurred on giving "myleran" (busulphan). The fourth patient, a man of 37, was diagnosed as suffering from chronic myeloid leukaemia. He responded satisfactorily to deep *x* rays to the spleen, but 5 months later the leucocyte count had again increased and the haemoglobin level had fallen. A satisfactory initial response occurred to colcemid therapy and this was maintained with 6 mg. in divided doses. Unfortunately, the platelet count fell and administration of the drug was stopped after a symptom-free remission of 5 months. After a further rise in leucocyte count a short remission was obtained by irradiation. Colcemid therapy was again tried and the leucocyte count fell, although the haemoglobin level did not rise. The treatment, however, resulted in severe generalized loss of hair, and since a generalized marrow aplasia was diagnosed, further treatment with cytotoxic drugs was considered to be contraindicated. All other measures taken proved ineffective and the patient subsequently died.

The authors' opinion is that, because of the distressing side-effect of depilation, colcemid should not be used in the treatment of chronic myeloid leukaemia unless the patient no longer responds to splenic irradiation and to myleran. *I. M. Rollo*

685. **The Effect of Massive Prednisone and Prednisolone Therapy on Acute Leukemia and Malignant Lymphomas**
H. M. RANNEY and A. GELLHORN. *American Journal of Medicine* [*Amer. J. Med.*] **22**, 405–413, March, 1957. 2 figs., 5 refs.

In this paper from Columbia University College of Physicians and Surgeons, New York, are reported the results of intensive treatment with prednisone and prednisolone of 24 patients (aged 8 to 70 years) with acute or subacute leukaemia and 10 patients (aged 32 to 65 years) suffering from malignant lymphomata. Both drugs were administered by mouth in doses of 0·25 g. every 6 hours.

Out of 18 patients with acute leukaemia, 5 had a temporary complete remission with a return of the peripheral blood to normal values and less than 10% blast cells in the marrow, and 6 a partial remission. Whereas complete remission was definitely related to the administration of the drug, this was not always the case with partial remission, which in 2 patients followed cessation of steroid therapy. Of the 11 patients in whom there was a remission, 4 are dead and 6 were known to be alive from 1 to 7 months after the start of therapy. In the remaining 7 cases of acute leukaemia no benefit was obtained, but in only one case was possible acceleration of the leukaemic process noted.

Of 6 cases of subacute leukaemia, which included 2 cases of chronic myeloid leukaemia in the acute myeloblastic phase, a transient remission was obtained in 2 only. The others showed no response, while in 2 cases there was possible acceleration of the disease.

Of 10 patients with lymphosarcoma who received massive steroid therapy, decrease of the tumour masses was noted in all save one, but this improvement persisted only so long as therapy was continued. Only one patient is alive 12 months after starting treatment.

Side-effects of steroid therapy were severe and often occurred within 10 days of starting treatment. They included increased nervous tension, psychosis, perforating peptic ulcer, hypokalaemia, and diabetes mellitus. The most dangerous was infection, both bacterial and fungus infection being encountered.

The authors are as yet uncertain of the place of massive steroid therapy in the acute leukaemias, but they do not recommend it as the treatment of choice, in view of the severe side-effects and the temporary nature of the remissions produced. For the same reasons they do not think that it is worth while giving this treatment in subacute leukaemia or in the malignant lymphomata. *D. G. Adamson*

Respiratory System

686. **Mucoid Impaction of the Bronchi**
A. E. GREER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 506–522, March, 1957. 14 figs., 2 refs.

Mucoid impaction of the bronchi complicates long-standing bronchial asthma and obstructive bronchitis and is due to the deposition of inspissated mucus in dilated bronchi. In this paper the clinical syndrome is described and the radiological appearances are discussed in detail [with helpful illustrations] with reference to cases reported in previous publications and to 5 cases seen personally by the author.

The upper lobes are the most frequently affected, the author's 5 cases all involving upper lobes. This predilection for the upper lobe is in contrast to the most usual site of bronchiectasis. Post mortem the dissected lungs show huge bronchi containing plugs of putty-like mucus; in some areas viscid clear mucus may be present peripheral to these masses. Microscopically, areas of granulomatous reaction can be identified and, when secondary infection has been predominant, acute and chronic inflammation will be evident. The symptoms of mucoid impaction of the bronchi are similar to those of asthma or chronic obstructive bronchitis. The expectoration of mucoid plugs is helpful in the diagnosis. Physical examination is not of much help. Radiographs of the chest may show characteristic shadows, but these may be indistinguishable from those due to simple inflammatory lesions, tuberculous infection, or neoplasm.

Treatment consists in the administration of antibiotics and potassium iodide. Bronchoscopy is of aid in excluding a visible endobronchial lesion, but is of no help in evacuating the plugs. The indications for surgery (lobectomy or segmental resection) are persistent pulmonary suppuration, repeated haemoptysis, and the need to obtain an exact diagnosis. Operation is contra-indicated by severe underlying pulmonary disease, involvement of multiple areas, or cor pulmonale.

A. I. Suchett-Kaye

687. **Failure of Penicillin to Prevent Post-operative Chest Infection**
E. GRIFFITHS. *British Medical Journal* [*Brit. med. J.*] **1**, 803–804, April 6, 1957. 3 refs.

In the last few years penicillin has been used to prevent postoperative pulmonary complications, and the author has attempted to assay the effectiveness of this routine. Over a period of 18 months patients undergoing operation in alternate months were treated with penicillin, while those operated on in the intervening months received no such prophylaxis. Patients admitted for emergency operations, also those who might in any case need antibiotics for operations involving the gut, were excluded. Operative procedures were mostly of a moderately minor order, and were comparable in type in both groups. The penicillin was given in a mixture containing procaine benzylpenicillin, 300,000 units, crystalline benzylpenicillin, 100,000 units, and dibenzylethylenediamine dibenzyl penicillin, 200,000 units, and was administered at the same time as the routine preoperative injection.

Patients were examined before the operation and again in the postoperative period and assigned to one of 5 groups on each occasion. Group 1 consisted of those without respiratory disease, and the remaining groups ranged from those with cough only (Group 2) to those with frank physical signs of consolidation or collapse (Group 5). If a patient's postoperative category was lower by one than that assigned preoperatively he was considered to have mild postoperative pulmonary complications; a lowering of category by more than one represented severe postoperative complications. Categories were assigned almost exclusively on the results of clinical examination.

[This investigation appears to have shown quite conclusively that preoperative penicillin does not significantly reduce the incidence of postoperative pulmonary complications. It is to be hoped that this paper will be widely read and in part help to reduce the prevalent indiscriminate use of prophylactic penicillin.]

J. N. Harris-Jones

688. **A Limited Clinical, Pathologic, and Epidemiologic Study of Patients with Pulmonary Lesions Associated with Atypical Acid-fast Bacilli in the Sputum**
H. E. CROW, C. T. KING, C. E. SMITH, R. F. CORPE, and I. STERGUS. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **75**, 199–222, Feb., 1957. 3 figs., 14 refs.

A study has been made of 69 patients with pulmonary disease admitted to the Battey State Hospital, Rome, Georgia, over a 5½-year period from whose sputum atypical acid-fast bacilli had been isolated. These cases comprised about 1% of the total admissions during this period. Most of the patients were white and over 40 years of age; 80% of them had no family history of tuberculous infection, and 67% gave a positive skin reaction to old tuberculin.

The bacilli in 64 instances showed similar morphological and cultural characteristics, and all were easily distinguishable from saprophytic mycobacteria. Tests for cord formation and neutral-red reduction gave inconclusive results; 53% of 19 strains were wholly or partially resistant to isoniazid, but only 12·5% of 32 strains showed any resistance to streptomycin. Only 2 out of 47 strains produced progressive disease when inoculated into guinea-pigs, while in 21 further instances there was limited disease confined to a local abscess or enlarged lymph nodes.

The results both of chemotherapy and of surgical treatment were moderate. The outcome of surgery in

13 cases was fairly satisfactory, the resected specimens from 7 of these patients showing a histological picture indistinguishable from that of infection with *Mycobacterium tuberculosis*. In only 24 instances did sputum culture become negative for 3 months or longer by all methods of treatment; there have been 7 deaths in the series from progressive pulmonary disease.

Problems of treatment and disposal are discussed. The authors feel that, while there is more indication for resort to surgery in these cases, the general plan of management should be as for a case of infection with *M. tuberculosis*. This should also apply to public-health precautions, even though such information as is available seems to indicate a lessened degree of infectivity.

John M. Talbot

689. **Drill Biopsy in Intrathoracic Malignant Disease**
R. MORRISON and T. J. DEELEY. *Thorax* [*Thorax*] **12**, 87–90, March, 1957. 6 figs., 6 refs.

Histological diagnosis of thoracic malignancy can often be obtained by bronchoscopy, but not when the lesion lies peripherally. The authors use a rotating hollow needle, driven by compressed air and 7 cm. long, for the biopsy of peripheral lung and pleural tumours under local analgesia. Precautions are taken to minimize the entry of air into the pleural space, but apparatus to deal with tension pneumothorax should be at hand.

Of 36 patients, 32 with pulmonary and 4 with pleural lesions, satisfactory biopsy material was obtained from 30, of whom 23 had malignant conditions. One patient developed a tension pneumothorax, but there were no cases of haemothorax, dissemination of tumour, or recurrence in the needle track. Failure may be due to inaccurate location, or the tumour may be too soft or too necrotic to provide a satisfactory specimen.

M. Meredith Brown

690. **The Results of Raising the Resectability Rate in Operations for Lung Carcinoma**
R. A. SMITH. *Thorax* [*Thorax*] **12**, 79–86, March, 1957. 7 figs., 8 refs.

In this article from King Edward VII Memorial Hospital, Warwick, the author attempts to determine whether lung resection affords worthwhile relief in those cases of cancer of the lung in which complete removal of the tumour is not possible. To this end he has studied 147 consecutive cases of carcinoma of the lung in which thoracotomy was performed, pneumonectomy or lobectomy being carried out in 143 (97·2%). A complete follow-up was achieved. In 95 cases the tumour with all its extensions and any involved lymph nodes appeared to have been resected completely. In 48 unmistakable tumour tissue was not completely removed because of its inaccessibility. The resectability rate by the ordinary standards was thus 70%. As palliative resection involves cutting across malignant tissue, the state of the bronchus is the most important factor to be taken into consideration, since division of an invaded main bronchus, especially the left, may be followed by fistula. The vessels can nearly always be secured in some way, usually after extensively opening the pericardium, though division of the pulmonary artery often involves proximal clamping and suture. A large number of sutures, tied not too tightly, will control bleeding from an artery extensively invaded by soft growth, while the pulmonary veins may be dealt with by clamping and suturing the left atrium, which may contain growth. Prolonged survival is possible after such operations. On the other hand attempts to remove growths invading the superior vena cava are rarely successful.

Of the 48 patients undergoing palliative resections, 10 died in hospital. Of the survivors, one-half lived more than 8 months and returned to work, while one was working 26 months after the operation. Only 2 were in hospital more than 16 days after operation. Sputum and haemoptysis were relieved, but it was not possible to assess the effect on pain. The terminal illness was usually short, death often being due to cerebral metastases.

The author does not advocate any alteration in the indications for limiting intervention to exploratory thoracotomy, but considers that when operation is undertaken, even if curative resection is impossible, it is desirable to carry out a palliative resection whenever possible.

M. Meredith Brown

691. **Role of Occupational and Environmental Air Pollutants in Production of Respiratory Cancers**
W. C. HUEPER. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] **63**, 427–450, May, 1957. 9 figs.

692. **Review of 464 Cases of Carcinoma of Lung Treated by Resection**
J. H. GIFFORD and J. K. B. WADDINGTON. *British Medical Journal* [*Brit. med. J.*] **1**, 723–730, March 30, 1957. 5 figs., 14 refs.

The authors have reviewed all the cases of bronchial carcinoma admitted to the Thoracic Surgical Unit at Broadgreen Hospital, Liverpool, between 1941 and 1954, amounting in all to 2,156. In 714 of these exploration was carried out and in 464 (21%) the growth was removed. A steadily increasing proportion of all cases registered in the area was admitted, reaching 45% in 1954. As the series progressed the proportions of patients admitted who underwent exploration and from whom the tumour was removed also increased steadily.

The operative mortality (within 2 months of operation) in the whole series was 21·7%; it was found to be twice as great when the tumour was on the right side as when it was on the left. Of the 204 patients who died subsequently, 74% were known to have had metastases, and the peak period for death from this cause was 18 months after the operation. The 5-year survival rate was 28%, that for left-sided tumours being 22% and that for right-sided tumours 34%. The lymph nodes were found to be involved in 38% of left-sided and only 28% of right-sided cases. The 5-year survival rate when the nodes were not involved was 33%, and with involvement 8%. Prognosis was best with squamous-celled tumours and worst with adenocarcinomata, but the length of the history before operation did not appear to have much influence on the survival rate. The patients who were subjected to pneumonectomy had a

better prognosis than those who underwent lobectomy, the 5-year survival rates being 29% and 12% respectively. *J. R. Belcher*

693. **Alveolar Carbon Dioxide Measurements in Normal and Emphysematous Subjects**
J. E. KELSEY, E. C. OLDHAM, and S. M. HORVATH. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **99**, 411–417, March, 1957. 4 figs., 9 refs.

The ventilatory response to the inhalation of carbon dioxide and the concentration of carbon dioxide in alveolar gas at rest and after hyperventilation were measured in a group of 22 emphysematous and 20 normal subjects at the Veterans Administration Hospital, Des Moines, Iowa. The age range (approximately 25 to 65 years) was similar in the two groups of subjects. [The sex distribution of the subjects is not stated, but they were presumably mostly or entirely male in view of the nature of the hospital. The age distribution, basis of diagnosis, and likely degree of emphysema are not specified.] The maximum voluntary ventilation (M.V.V.) over 20 seconds and resting minute volume were measured with a Tissot spirometer, also the vital capacity and 3-second vital capacity [3-second forced expiratory volume (F.E.V.)]. Both the maximum and the average concentration of carbon dioxide in expired gas were determined with a Liston–Becker infra-red carbon dioxide analyser, and the effects of inhalation of air, oxygen, and 2·5% and 7·5% carbon dioxide in oxygen were all studied.

There was a statistically significant difference between the average M.V.V. and F.E.V. for the two groups. The average ventilation of both groups increased on inhalation of carbon dioxide, the increase in the normal group being threefold, compared with a twofold increase in the emphysematous subjects. After the 20-second M.V.V. tests the alveolar tension of carbon dioxide fell by an average of only 6 mm. Hg in the emphysematous group compared with 9·6 mm. Hg in the normal group. The authors conclude that the smaller ventilatory response to carbon dioxide in emphysema results from the mechanical limitations on ventilation in that condition, which is shown by the reduction in M.V.V., rather than from a decreased sensitivity of the respiratory centre to carbon dioxide. This deduction is based on the facts that none of their subjects failed to respond to carbon dioxide; that the emphysematous subjects used, on the average, two-thirds of their maximum ventilatory capacity in their response, and the normal subjects one-third; and that the percentage increase in alveolar carbon dioxide concentration when the subjects inhaled the carbon dioxide mixtures was linearly related to the percentage increase in minute ventilation (over the corresponding values when breathing air) in both groups of subjects. The authors conclude that the M.V.V., timed vital capacity, alveolar carbon dioxide concentration at rest and after the M.V.V. test, and the ventilatory response to breathing 7·5% carbon dioxide in oxygen are all useful measurements for distinguishing emphysematous from normal subjects.

[Cherniack and Sindal (*J. clin. Invest.*, 1956, **35**, 1286) likewise concluded that the smaller ventilatory response to carbon dioxide inhalation in emphysema resulted primarily from mechanical limitation of ventilation in that condition rather than from an insensitive respiratory centre.] *P. Hugh-Jones*

694. **Acute Spontaneous Mediastinal Emphysema**
S. G. F. MATTS. *Lancet* [*Lancet*] **1**, 507–510, March 9, 1957. 2 figs., 48 refs.

This paper from the Royal Devon and Exeter Hospital describes 3 cases of non-traumatic mediastinal emphysema. In the first case a 4-year-old boy with measles developed a cough and increasing breathlessness on the 3rd day after the emergence of the rash, becoming acutely dyspnoeic on the 4th day, when he was admitted to hospital. On examination he was ill and slightly cyanosed, with a temperature of 100·8° F. (38·2° C.), respirations 60 per minute, and gross surgical emphysema all over his chest extending into both sides of his neck and face. Moist rales were heard on both sides of the chest. *X* rays showed surgical emphysema of the chest wall, mediastinum, and both axillae, consolidation in the middle zone of the left lung, but no pneumothorax. Under treatment with oxygen, sedation, and full doses of tetracycline, the emphysema was absorbed in 4 days and recovery was uneventful. The diagnosis was of atelectasis due to broncho-pneumonia, with over-inflation due to coughing causing the mediastinal emphysema. In the second case a healthy male bank clerk of 17 was admitted to hospital with severe constricting pain in the throat, front of the chest, epigastrium, and left side, of sudden onset 5 minutes after drinking a glass of " fizzy lemonade ". He was found to have surgical emphysema of his left chest wall and neck and a to-and-fro " pericardial rub ". Radiography showed emphysema of the neck, left axilla, and mediastinum, with normal lung fields and no pneumothorax. Barium-swallow examination showed no abnormality. An uneventful recovery followed rest in bed, with penicillin and passage of a Ryle's tube which was left *in situ* for 36 hours, the emphysema disappearing after 10 days. The cause of the mediastinal emphysema in this case was unknown. In the third case, while gastrectomy was being performed on a man of 35, the emergency oxygen supply was accidently turned on for about 1 to 2 minutes with the expiratory valve of the anaesthetic mask almost closed. The surgeon found much surgical emphysema in the mesentery of the transverse colon, but the operation was completed normally, the emphysema meanwhile rapidly resolving. There was slight surgical emphysema of the neck which resolved in a day or two, but no signs in the chest. The patient made an uneventful recovery.

The author emphasizes the relatively mild symptoms, the minimal physical signs (in 2 cases), and the rapid recovery from this condition. The possible portals of entry of air into the mediastinum are discussed in detail and all the conditions, traumatic and non-traumatic, in which mediastinal emphysema has been reported or in which the known predisposing factors may be present are listed. It is suggested that mild cases may be missed, and the importance in diagnosis of a lateral radiograph of the chest is stressed. *L. G. Fallows*

Otorhinolaryngology

695. **Therapeutically Induced Paralysis of the Cricothyroid Muscle or Its Removal in Paralytic Laryngeal Stenosis**

K. TSCHIASSNY. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **65**, 133–142, Feb., 1957. 40 refs.

After discussing the validity of Semon's law concerning the effects on the larynx of a progressive lesion of the recurrent laryngeal nerve in the light of recent observations the author expresses his own views. He groups the laryngeal muscles as tensors, abductors, and adductors and considers that so far as respiration is concerned the influence of the tensors is negligible. He states that in quiet respiration, both abductors and adductors are relaxed and the cords lie in the cadaveric position; in forced expiration the abductors are relaxed and the adductors active, and the cords lie in the median position; while in forced inspiration the adductors are relaxed and the abductors active, and the cords lie in the lateral position. Arguing from this, he does not admit that there is a muscle group which can be described as the "opener of the glottis", and in support of this he quotes experimental findings over many years. He concludes that the abductors are the "dilators" of the larynx, not the "openers". The larynx is opened by inhibition of adductor tonus and by the elastic force of the membrana elastica laryngis inferior (the "conus elasticus").

Hence as the abductors are not the "openers" of the larynx, the inability of the glottis to open in so-called "bilateral abductor paralysis" is not due to the paralysis. It may be due to degeneration of the joints and ligaments or to spasm of the unaffected cricothyroid muscle, which is not supplied by the recurrent laryngeal nerve. Therefore if the joints and ligaments preserve normal function and the cricothyroid muscle has not degenerated, elimination of that muscle, either by its removal or by division of the superior laryngeal nerve may allow the cords to fall into the cadaveric position. This, in suitable cases, would replace the operations now used for altering the position of the cords and so reopening the airway. *F. W. Watkyn-Thomas*

696. **Observations on the Surgery of the Nasopharynx**

C. P. WILSON. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol. (St Louis)*] **66**, 5–40, March, 1957. 20 figs., 24 refs.

In this article the author advocates the wider use of his well-known technique of approach to the nasopharynx through the soft palate. He describes this approach as a means of investigating the nasopharynx for carcinoma and he mentions 5 cases in which a positive diagnosis of carcinoma was made by biopsy although there were no visible signs of a tumour, even after division of the soft palate. He is, however, no longer in favour of fenestration of the palate as an adjunct to radiotherapy in such cases, considering that radiotherapy alone holds out the best hope of success.

A nasopharyngeal fibroma can be dealt with through this approach, his practice being to give a course of radiotherapy first and to follow with a palatal fenestration 6 weeks later, when the fibroma is excised. The opening is closed with an obturator, which may have to be changed at intervals as the patient grows, most of these tumours occurring in young boys.

In unilateral or bilateral choanal atresia, where the problem is not urgent, the nasopharynx can be approached through a palatal fenestration, though care must be taken to keep the mucous membrane intact. In removing the bone or fibrous tissue which causes the atresia, part of the posterior part of the bony nasal septum should be removed as well. The mucous membrane is then cut in flaps and arranged to cover the raw surfaces immediately adjacent to the atresia.

William McKenzie

697. **Clinical Determination of Abnormal Auditory Adaptation**

R. CARHART. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **65**, 32–39, Jan., 1957. 9 figs., 10 refs.

Hallpike and Hood have distinguished between the "on-effect"—the first burst of auditory excitation—and "adaption"—the progressive reduction in response to continued stimulation. They claim that recruitment is diagnostic of an end-organ lesion and occurs because the "on-effect" is essentially normal. Also, in Ménière's disease, which they regard as the prototype of end-organ lesions, "adaption" is abnormally rapid. This they describe as "relapse", and they regard a normal "on-effect" with "relapse" as proof that there is end-organ damage.

The present author does not believe that there is a "fixed relationship" between loudness and difference-limen for intensity change, so that tests based on difference-limen are not necessarily tests for recruitment. Many "recruitment tests" are based on this fallacy; others need special equipment, while the simple and satisfactory "balance of loudness" test is only applicable in special cases. The author suggests a new test which demonstrates the presence of "relapse". This he describes as "threshold tone decay test". A pure tone is delivered at threshold for one minute. If its perception fades out before that time, the intensity is raised by 5 db. No rest period is allowed. This is repeated until the tone is heard for the full minute, or until abnormal adaptation at threshold is clearly shown.

F. W. Watkyn-Thomas

Endocrinology

698. **Defective Organic Binding of Iodine by the Thyroid in Hashimoto's Thyroiditis**
M. E. MORGANS and W. R. TROTTER. *Lancet* [*Lancet*] **1**, 553–555, March 16, 1957. 5 figs., 13 refs.

An investigation is reported from University College Hospital, London, of the organic binding of radioactive iodine (^{131}I) in cases of simple goitre and cases of lymphadenoid goitre (Hashimoto's thyroiditis). A group of 12 patients believed to have Hashimoto's thyroiditis was studied; in 6 of these who had undergone thyroidectomy the diagnosis was confirmed histologically, and in 4 of the remainder there was a positive reaction to the serum flocculation test with a raised serum γ globulin level. Similarly studied were 26 cases of simple goitre (diffuse and nodular types) with normal thyroid function. A dose of 20 to 40 μc. of ^{131}I was given by mouth at least 5 hours after the last meal and counts were made with a Geiger counter simultaneously over the thyroid gland and thigh regions 50 and 60 minutes later. Immediately after the 60-minute count the patient drank a solution of potassium perchlorate containing either 200 mg. or 400 mg. in 25 or 50 ml. of water. Half the thigh count was subtracted from the neck count to compensate for the extra-thyroidal radioactivity. The values calculated in this way for thyroid radioactivity at 10, 20, 30, and 40 minutes were then expressed as a percentage of the thyroid radioactivity present immediately before the perchlorate was given.

When potassium perchlorate is given to healthy subjects one hour after a tracer dose of ^{131}I, the thyroid count increases slightly and then remains constant. In the 25 patients with simple goitre the reaction was similar to that of healthy subjects, but in the 12 patients with Hashimoto's thyroiditis there was a significant tendency for thyroid radioactivity to be discharged after administration of perchlorate. The authors discuss this finding and conclude that there is presumptive evidence of a partial defect in the organic binding of iodine by the gland in Hashimoto's thyroiditis. *Norval Taylor*

699. **The Effect of Phenylbutazone and a Related Analogue (G25671) upon Thyroid Function**
J. A. LINSK, B. C. PATON, M. PERSKY, M. ISAACS, and H. S. KUPPERMAN. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **17**, 416–423, March, 1957. 4 figs., 9 refs.

At the Goldwater Memorial Hospital and New York University–Bellevue Medical Center, New York, the uptake by the thyroid of radioactive iodine (^{131}I) was estimated in 13 euthyroid subjects before and after the administration of 800 mg. of phenylbutazone daily for 4 days. A consistent and marked reduction in ^{131}I uptake was observed in all cases, the fall being to levels ranging from 10 to 37% of the control level. The concentration of the drug in the blood was estimated in 8 cases and was found to be within the limits observed during its therapeutic use in rheumatic conditions. After discontinuation of the drug for 7 days the ^{131}I uptake had risen again to the control level in 2 out of 3 cases reinvestigated, and to 80% of that level (from 14%) in the third case.

The authors note that in spite of this demonstrable suppression of thyroid activity phenylbutazone does not produce hypothyroidism or goitre when given for long periods. They therefore reinvestigated ^{131}I uptake in 4 patients who had been given phenylbutazone continuously for periods ranging from 16 to 97 days. From these studies it appears that the thyroid-inhibiting effect of the drug begins to wear off after 4 days, although there may be some residual effect even after 97 days. To determine the mode of action of phenylbutazone it was administered together with pituitary thyroid-stimulating hormone (T.S.H.) in 3 of the cases previously investigated. It was found that the inhibiting action of the drug was abolished by the subcutaneous injection of 10 units of T.S.H. for 4 days. It is suggested that the drug probably acts by suppressing pituitary function.

An analogue of phenylbutazone, 4-(phenulthioethyl)-1: 2-diphenyl-3: 5-pyrazolidinedione was also investigated. In this a phenyl-thio-ethyl side-chain has been substituted for a butyl group. This drug was shown to have no thyroid-depressing effect, although it has some anti-inflammatory action and is said to be a powerful uricosuric agent. *T. D. Kellock*

700. **Parathyroid Damage in Man: Mechanism of Effect on Serum Levels of Calcium and Phosphorus**
S. M. KRANE. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **17**, 386–389, March, 1957. 8 refs.

In view of Munson's observation (*Ann. N.Y. Acad. Sci.*, 1955, **60**, 776) that after parathyroidectomy in rats the serum calcium level fell before any rise in phosphorus concentration, the author has investigated the serological changes recorded in patients at the Massachusetts General Hospital who developed tetany after thyroidectomy during the past 10 years. Altogether there were 10 patients who had developed signs of tetany within one to 4 days after thyroidectomy and whose blood had been analysed for both calcium and phosphorus before the start of treatment. In 6 cases the operation had been performed for diffuse toxic goitre, in 3 for carcinoma and in one for non-toxic nodular goitre. In all except 3 cases the hypoparathyroidism was permanent.

The serum calcium level at the time of onset of symptoms ranged from 4·9 to 7·6 mg. per 100 ml. In 6 cases the serum phosphorus concentration was below 4 mg. per 100 ml., and in only one of the other cases was it greater than 4·7 mg. per 100 ml.

It is concluded that these observations confirm those of Munson (and those made in 1924 by Greenwald) in animals and suggest that the secretion of the parathyroid glands has a direct effect on the serum calcium level rather than an indirect one through control of renal excretion of phosphates. *T. D. Kellock*

ADRENAL GLANDS

701. **Cushing's Syndrome: Failure to Demonstrate Diminished Peripheral Glucose Uptake and Insulin Resistance**

M. FABRYKANT, R. S. JACKSON, and B. I. ASHE. *Metabolism* [*Metabolism*] **6**, 116–126, March, 1957. 5 figs., 25 refs.

Four patients with Cushing's syndrome have been studied for 6 years at the University Hospital, New York. Their resistance to insulin (as revealed in insulin tolerance tests) and their ability to show a peripheral uptake of glucose after standard oral glucose tolerance tests were investigated, together with estimations of their urinary excretion of 17-ketosteroids and 11-oxysteroids. Results indicate that in Cushing's syndrome the glucose uptake by the tissues is normal or even enhanced, and a satisfactory fall in blood glucose level occurs during tests of insulin tolerance. A possible explanation for the derangement of carbohydrate metabolism seen in these patients is the overproduction of the adrenal glucocorticoids. *G. B. West*

702. **Preoperative Differentiation between Hyperplasia and Tumor in Cushing's Syndrome**

F. HINMAN, H. L. STEINBACH, and P. H. FORSHAM. *Journal of Urology* [*J. Urol.* (*Baltimore*)] **77**, 329–338, March, 1957. 6 figs., 11 refs.

In this paper from the University of California School of Medicine, San Francisco, the authors have analysed the usefulness of hormone excretion studies and of various radiological techniques in differentiating between adrenal hyperplasia and neoplasia in 20 cases of Cushing's syndrome coming to operation. A 17-hydroxycorticoid excretion rate of over 12 mg. per day was considered suggestive of Cushing's syndrome. After stimulation by an 8-hour intravenous drip of 20 units of corticotrophin the 14 cases of hyperplasia and 4 of adenoma gave levels of over 50 mg. per day, while the 2 cases of carcinoma showed no significant rise above the already high resting level. Levels of 17-ketosteroid excretion before and after stimulation were not considered to be of such diagnostic help as in purely virilizing syndromes. No reliable diagnostic information was obtained from studying the suppression of 17-hydroxycosticoid excretion by fluorocortisone acetate.

The authors did not find plain radiographs of the adrenal area to be of much help in diagnosis, and intravenous and retrograde pyelography were similarly disappointing. Displacement of the left kidney below the level of the right is considered unreliable, as this occurs in 15% of normal individuals. Presacral oxygen insufflation, together with tomography, is advocated, having been diagnostic in 18 of the 20 cases. It was found that a round or oval mass is virtually diagnostic of an adrenal neoplasm (adenoma or carcinoma) and an atrophic adrenal is very suggestive of contralateral neoplasia.

There was no correlation between the post-stimulation rate of excretion of 17-hydroxycorticoids and the radiological or operative size of the tumours or hyperplastic glands.

The authors conclude that: (1) adrenocorticotrophic hormone stimulation tests distinguish adrenal carcinomata from adrenal adenomata or hyperplasia in Cushing's syndrome, and (2) presacral pneumograms distinguish hyperplasia of the adrenals from neoplasia. *J. Warwick Buckler*

703. **Urinary Porter–Silber Chromogen versus Blue Tetrazolium Chromogen as a Quantitative Index of Adrenocortical Function**

L. J. MARKS, J. H. LEFTIN, and M. P. LEONARD. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **17**, 407–415, March, 1957. 2 figs., 13 refs.

The authors, working at the Boston Veterans Administration Hospital, have investigated the comparative merits of two different methods of assessing the urinary metabolites of the adrenocortical steroids. The phenylhydrazine–sulphuric acid reaction introduced by Porter and Silber (*J. biol. Chem.*, 1950, **185**, 201) is specific for determining steroids with both an alpha-ketol grouping and a hydroxyl group at the C_{17} position, but as some steroids, such as aldosterone and corticosterone, have no 17-hydroxyl groups they are not measured by this method. The method introduced by Mader and Buck (*Analyt. Chem.*, 1952, **24**, 666) based on the reduction of blue tetrazolium does not depend on the presence of the 17-hydroxyl group and can therefore be used for the estimation of steroids with only an alpha-ketol grouping at the C_{17} position in addition to those measured by the former method.

Urine for testing was hydrolysed with β-glucuronidase and extracted with chloroform; chromatography was performed on "florisil" columns, which were then eluted with chloroform, 4% methanol in chloroform, and finally 25% methanol in chloroform. The 24-hour urinary excretion of Porter–Silber chromogen (P.S.C.) and of blue tetrazolium chromogen (B.T.C.) was determined in 42 normal adult males, in 8 patients suffering from various endocrine diseases, and (after the intravenous infusion of 25 units of ACTH (corticotrophin)) in 5 male patients with possible adrenal insufficiency. In all these groups the correlation between urinary P.S.C. and B.T.C. excretion as measurements of adrenocortical function was poor. The authors consider that "it is doubtful [whether] urinary BTC is as specific a measure of urinary adrenocortical metabolites as is urinary PSC". *T. D. Kellock*

704. **An Investigation of the Action of Cortisone and Prednisone on Intravenous Glucose Tolerance.** [In English]

G. HOLTEN, K. LUNDBAEK, and I. STAFFELDT. *Acta medica Scandinavica* [*Acta med. scand.*] **157**, 257–262, May 4, 1957. 2 figs., 14 refs.

DIABETES MELLITUS

705. **Diabetic Vascular Changes in the Eye.** (Beiträge zur Kenntnis der diabetischen Gefässerkrankungen des Auges)
O. PALICH-SZÁNTO and G. BIKICH. *Ophthalmologica* [*Ophthalmologica (Basel)*] **133**, 109–118, Feb., 1957. 17 refs.

Diabetic vascular changes in the eye may be present: (1) in the conjunctiva, where micro-aneurysms may be found; (2) in the iris, as rubeosis iridis and in some cases of glaucoma; and (3) as diabetic retinopathy which ranges in extent from small petechiae and micro-aneurysms to retinitis proliferans. Occasionally thrombosis of the central vein is found. Diabetic systemic vascular changes occur in the kidneys, coronary vessels, cerebral vessels, and venous system. Of 101 diabetics studied by the authors at the János General Hospital, Budapest, retinopathy was found in 22; when the duration of the diabetes was between one and 10 years the incidence was 14%, while in the group with a duration of more than 10 years the frequency was 34%. Conjunctival aneurysms were found in 20% of cases, mostly in those of over 10 years' duration. In several cases 2 or more members of the same family with retinopathy were encountered, and among the affected patients blood-relationship of the parents was more frequent than in those without retinopathy. [No figures are given.]

M. Klein

706. **A Study of the Action of "Hypoglycaemic" Substances on a Group of 275 Diabetic Children.** (Étude de l'action des substances "hypoglycémiantes" sur un groupe de 275 enfants diabétiques)
H. LESTRADET, J. BESSE, and C. JEZEQUEL. *Presse médicale* [*Presse méd.*] **65**, 553–556, March 23, 1957. 2 figs., 43 refs.

The authors report the results of a study of the effects of oral hypoglycaemic drugs which was carried out at three colonies for diabetic children under the auspices of the Centre for the Study of Metabolic Diseases in Children, Paris. The method adopted was to compare the effects of the administration of different doses of the hypoglycaemic drugs on the mean insulin requirements of groups of children, using for control purposes similar groups in the same colony who at the same time received a placebo which appeared identical with the active drug. The groups varied in size from 13 to 25 children, and their mean ages from 8 to 14.

The drugs given were the sulphonamide derivatives "D860" (tolbutamide) and "2254 RP.", and 6 separate investigations were made with varying doses of the drugs. In no case was there any convincing evidence of an insulin-sparing action of the drugs. The results were as discouraging in children receiving very small amounts of insulin as they were in others, nor had the duration of the diabetes any relation to the result.

One child of 5 showed a remarkable improvement in that his requirements fell from 25 units of protamine zinc insulin daily to *nil* in 2 weeks, but this was presumably due to the effects of an athletic life as he was receiving the placebo! The authors point out that such spontaneous changes should make one very cautious in assessing the results of treatment in isolated cases.

T. D. Kellock

707. **Clinical Studies of the Hypoglycaemic Action of the Sulphonylureas**
W. J. H. BUTTERFIELD, J. L. CAMP, C. HARDWICK, and H. E. HOLLING. *Lancet* [*Lancet*] **1**, 753–756, April 13, 1957. 1 fig., 27 refs.

An investigation of the hypoglycaemic action of the sulphonylureas carbutamide and tolbutamide, which was carried out under the auspices of the Medical Research Council in collaboration with the Diabetic Department of Guy's Hospital, is reported. A group of 29 diabetic patients were treated for 7 days with a sulphonylurea (with and without insulin) in a dosage initially of 3 to 4 g. daily, followed by 2 to 3 g. daily. Various carbohydrate-tolerance tests were carried out, and the arteriovenous differences in blood sugar level, the peripheral blood flow, and the hyperglycaemic response to injection of glucagon were studied in all cases. The fasting blood sugar level fell more than 15% in 22 patients. Clinical and statistical analysis of the results did not reveal any evidence that the hypoglycaemic action of the sulphonylureas "was mediated by any of the mechanisms so far suggested by the results of experiments in animals". In the authors' view "the predominant changes occur in the mechanisms controlling the fasting blood-sugar level, and that all other factors are essentially unaffected".

A. I. Suchett-Kaye

708. **Glucose-6-Phosphatase Activity in Human Diabetes**
S. J. PATRICK and J. A. TULLOCH. *Lancet* [*Lancet*] **1**, 811–812, April 20, 1957. 13 refs.

The authors describe an investigation of the glucose-6-phosphatase activity of the liver before and after therapy in a group of 13 diabetics at University College Hospital of the West Indies, Jamaica. The series consisted of 2 young acute diabetics who were insulin-resistant and poorly controlled, 3 insulin-sensitive patients, and 8 middle-aged or elderly diabetics who were underweight and insulin-resistant. Also investigated were 7 non-diabetic subjects. Liver biopsy was performed with a Vim–Silverman needle at about 9 a.m. when the subject was fasting. Specimens were immediately frozen in solid carbon dioxide, and assays of enzyme activity were made by a micro-method which is described in detail. One unit of glucose-6-phosphatase activity was estimated as equivalent to one micromol of inorganic phosphate liberated per mg. of liver nitrogen per minute.

In the 13 diabetics the average enzyme activity before therapy was 0·271 unit (range 0·175 to 0·397 unit), and after therapy with insulin, or in 2 cases with carbutamide, it was 0·175 unit (range 0·141 to 0·214 unit). In the 7 non-diabetics the average enzyme activity was 0·155 unit.

It was concluded that in the diabetics there was an increased activity of the enzyme in the liver as compared with the non-diabetics, and in all the diabetics the enzyme activity was decreased when the diabetes was stabilized by treatment with insulin or carbutamide.

Charles Rolland

The Rheumatic Diseases

709. **Variations in the Blood Cholesterol Level during Acute Attacks of Rheumatic Fever.** (Les variations du cholestérol sanguin au cours de la poussée aiguë de la maladie de Bouillaud)
H. KAUFMANN and P. ISORNI. *Presse médicale* [*Presse méd.*] **65**, 600–601, March 30, 1957. 1 fig., 10 refs.

In investigations carried out at the Hôpital de Versailles the concentrations of total cholesterol, cholesterol esters, and free cholesterol in the blood were measured frequently during the course of the illness in 10 patients with acute rheumatism and in 2 patients with mitral stenosis and manifestations suggesting active rheumatic carditis. It was found that during the active phase of the disease the total cholesterol and cholesterol ester levels in the blood were low, and that these rose during convalescence. In fact the blood cholesterol level varied inversely with the erythrocyte sedimentation rate. The total cholesterol content of the blood in early convalescence was about 100% above that in the acute phase. It subsequently fell, but not to the original value. The significance of this change in the level of blood cholesterol is obscure, but it is suggested that the determination of the blood cholesterol content may be of help in assessing the progress of the disease.

[It should be noted that all the patients studied were receiving treatment with " deltacortisone ".]

C. Bruce Perry

710. **Prevention of Attacks of Gout with Phenylbutazone.** (Prevención de los ataques gotosos por la fenilbutazona)
A. R. MORENO. *Archivos argentinos de reumatología* [*Arch. argent. Reum.*] **19**, 188–193, Sept.–Dec., 1956. [Received April, 1957.]

At the Anti-rheumatism Centre of the Faculty of Medical Science, Buenos Aires, the author treated 22 men aged 42 to 70 with gout of 7 or more years' duration, each of whom had had 4 or more attacks in the preceding year, with 100 to 200 mg. of phenylbutazone daily for 1 to 2 years. A similar group of 22 men with gout who received intermittent medication during attacks only served as controls. In addition, 10 patients with gout were given continuous, then intermittent, then continuous medication in consecutive years.

Only 7 attacks of gout occurred during the first year of the trial in the group of 22 men receiving phenylbutazone continuously, as opposed to 88 attacks in the control group. In the group receiving alternating methods of medication the total number of attacks in the year before the trial was 47; in the first and third years (continuous medication) there were 3 attacks; and in the second year (intermittent medication) 40 attacks. No toxic effects were seen, routine leucocyte counts and urine examination being carried out. There was no effect on the hyperuricaemia. The author concludes that continuous treatment of gouty patients with small doses of phenylbutazone can safely be undertaken and will prevent recurrences of acute gout. [Data on the comparability of the treatment groups are not given.]

Allan St. J. Dixon

CHRONIC RHEUMATISM

711. **Digital Cysts Associated with Heberden's Nodes (Cystic Mucoidosis).** (Quistes digitales para-heberdianos (mucoidosis quística))
H. BARCELO. *Archivos argentinos de reumatología* [*Arch. argent. Reum.*] **19**, 200–207, Sept.–Dec., 1956. 7 figs., 7 refs.

From the Anti-rheumatism Centre of the Faculty o Medical Science, Buenos Aires, the author describes small cystic swellings occurring adjacent to Heberden's nodes in 6 patients with osteoarthritis. One of these cysts was removed, and on histological examination showed replacement of collagen, reticulin, and elastic fibres by clear mucoid. The mucoid could be broken down by hyaluronidase. The skin over the cysts was atrophic and had lost the normal papillae, while the basement membrane was discontinuous. A fibroblastic and cellular proliferation encapsulated the cyst. He briefly reviews the literature, notes that the cysts do not communicate with the terminal interphalangeal joint, and concludes that they represent a reaction of the skin to the pressure on the corium of the underlying bony prominence.

Allan St. J. Dixon

712. **Phenylbutazone. Effects of Its Administration for Prolonged Periods**
W. C. KUZELL, R. W. SCHAFFARZICK, W. E. NAUGLER, and B. M. CHAMPLIN. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 388–392, Feb. 28, 1957. 3 refs.

At Stanford University School of Medicine, San Francisco, the effects of prolonged administration of phenylbutazone were studied in 100 patients—60 with rheumatoid arthritis, 23 with ankylosing spondylitis, 4 with arthritis and psoriasis, and 13 with mixed arthritis. The daily dose of the drug ranged from 100 to 600 mg., but most patients received 300 to 400 mg. daily, and the duration of the treatment varied from 12 months to 4½ years.

Initially there was a Grade-I response (complete remission) or a Grade-II response (major improvement) in 91 patients; the initial response in the remaining 9 was Grade III (minor improvement). The original favourable response was maintained throughout the period of treatment in 90 patients. Toxic effects included rash (3 cases), stomatitis (5), dyspepsia (15), vertigo (2), transitory visual blurring (2), purpura (2), and agranulocytosis (2). Administration of the drug was successfully resumed later in all these patients. One patient died from haemorrhage from a duodenal ulcer.

Laboratory examination at the end of the period of study did not reveal any abnormality of the blood cells or any evidence of hepatic damage. *C. E. Quin*

713. **The Simultaneous Occurrence of Rheumatoid Arthritis and Agammaglobulinemia**
R. A. GOOD, J. RÖTSTEIN, and W. F. MAZZITELLO. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **49**, 343–357, March, 1957. 6 figs., 29 refs.

Agammaglobulinaemia is a rare condition characterized clinically by repeated attacks of bacterial infection, resulting from a gross immunological defect. From the 58 cases so far reported there appear to be two forms—congenital, occurring in children, and acquired, in which the lack of response to infection appears in later life. In several of these reported cases " rheumatic " symptoms were noted—for example, joint pain and tenosynovitis—and in 8 there appeared to be rheumatoid arthritis. The authors describe 3 cases—2 in which the condition was apparently acquired in adult life and one, in a child, of congenital agammaglobulinaemia. The association of agammaglobulinaemia with other " collagen " diseases—scleroderma, dermatomyositis, and (probably) disseminated lupus erythematosus—is discussed.

The authors point out that the pathogenesis of rheumatoid arthritis has been much related, in theory, to some form of hypersensitivity, to antibody formation, or to disturbance of gamma-globulin metabolism. The fact that rheumatoid arthritis can coexist with agammaglobulinaemia makes theories involving anaphylactic or immunological mechanisms less attractive, if not untenable. In patients with agammaglobulinaemia, however, bacterial allergy does develop in spite of the defect, and it is therefore still possible that rheumatoid arthritis may have an allergic basis. *B. E. W. Mace*

714. **Latent Haemolysis in Rheumatoid Arthritis**
P. C. MCCREA. *Lancet* [*Lancet*] **1**, 402–406, Feb. 23, 1957. 45 refs.

An inquiry into the nature of the anaemia associated with rheumatoid arthritis was carried out at the Royal Bath and White Hart Hospital, Harrogate, in which 15 in-patients with active rheumatoid arthritis were studied. The erythrocyte life-span was measured by Dacie and Mollison's modification of Ashby's technique, cells from 800 to 1,200 ml. of blood being transfused and the normal life-span of the erythrocyte being taken as 100 to 120 days. In 10 of the cases studied the rate of erythrocyte destruction was increased, the life-span varying from 30 to 90 days. The serum bilirubin level and the reticulocyte count were within normal limits with a single exception. The faecal urobilinogen content and the osmotic fragility of the erythrocytes were determined in 6 cases and were normal in all. In 5 of 7 cases stainable iron was demonstrated in the sternal bone marrow and there was no response to intravenous iron therapy, the increase in haemoglobin level being less than 2 g. per 100 ml. of blood.

It is concluded that " latent haemolysis, demonstrated by abnormally short survival-time of normal red cells, is a factor in the production of anaemia in certain cases of active arthritis ". In addition, the bone-marrow response to haemolysis in these cases was less than would be expected if marrow function was normal, and erythrocytes were produced that were deficient in haemoglobin, this deficiency not being apparently due to a lack of iron. There is an extensive discussion of the literature of these and related phenomena. *Harry Coke*

715. **Streptohaemagglutination in Rheumatoid Arthritis**
H. BEEUWKES, A. BIJLSMA, and D. E. MENDES DE LEON. *Acta medica Scandinavica* [*Acta med. scand.*] **157**, 119–128, March 25, 1957. 8 refs.

Rose's test and the L-agglutination test are known to be of value in the diagnosis of rheumatoid arthritis of long standing. The authors now describe in detail a method by which it is possible to support the early diagnosis of rheumatoid arthritis. By extraction of β-streptococci Type 3 (Lancefield Group A) with acetamide, an extract was obtained which gave positive haemagglutination in 21 (71·8%) of 32 samples of serum from patients with Stage-I rheumatoid arthritis. Rose's test was positive at this stage in only 5·1%. As control sera, donor's blood from the transfusion service was used and 20% of 90 such sera gave a positive streptohaemagglutination reaction.

In the late stages of rheumatoid arthritis the proportion of positive reactions with this method was approximately the same as in the early stages, while the percentage of positive results in the Rose and L-agglutination test increased. Both complete and incomplete antibodies were demonstrated, and a complement-fixation test using the streptococcal extract gave a positive result in some patients though it seemed to be less sensitive than the streptohaemagglutination reaction. The authors state that the streptococcal extract is not group-specific, since it reacts to sera of Groups A, C, and D. It is thermolabile and in this, as in some other characteristics, it is similar to the so-called L-antigen. *G. W. Csonka*

716. **Pancreatic Necrosis in a Case of Still's Disease**
M. MARCZYNSKA-ROBOWSKA. *Lancet* [*Lancet*] **1**, 815–816, April 20, 1957. 10 refs.

717. **Radiological Study of Sacro-iliac Joints in Ankylosing Spondylitis with Reference to the Evolution of the Disease**
J. FORESTIER and P. DESLOUS-PAOLI. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **16**, 31–34, March, 1957. 4 figs., 8 refs.

In this paper from Aix-les-Bains, France, a study is reported of 300 cases of ankylosing spondylitis which were observed for periods ranging from 6 to 23 years, special attention being directed to the radiological appearances of the sacro-iliac joints. From this study the following conclusions were reached.

For a period of 5 to 7 years after the apparent onset of ankylosing spondylitis marginal decalcification may be observed. The bony contours are hazy, and the joint spaces appear to be wider than normal. There may be two vertical areas of bony condensation in the subchondral zones of the sacrum and ilium. These changes

constitute the first stage in the evolution of the disease. The second stage is characterized by joint erosion, reconstruction of the adjacent bone, and pronounced bony condensation with mottling. In the third stage the radiological appearances are not specific to ankylosing spondylitis. There is bony fusion of the lower two-thirds of the joint space, but condensation of the bone is no longer visible. When the disease is of long standing, fine bony streaks may be seen crossing the sacro-iliac space obliquely and disappearing in the vicinity of the upper part of the acetabulum.

Irrespective of the age or sex of the patient any stage may be encountered 8 to 15 years after the onset of the disease. Bony ankylosis develops from 7 to 23 years after onset, but its appearance is not a sign that the evolution of the disease has ceased. Clinically, the disease remains active for an average of 19 years. If the erythrocyte sedimentation rate is normal for 2 years and there has been no spinal or referred pain for a similar period, it is justifiable to conclude that all activity has been arrested. Usually ankylosing spondylitis begins at puberty, and the evolution of the disease is completed during the period of sexual activity. In contrast, rheumatoid arthritis may begin at any age.

A. Garland

COLLAGEN DISEASES

718. **Disseminated Lupus Erythematosus. A Clinical Study of Thirteen Cases.** (Le lupus érythémateux disséminé. (Étude clinique de treize cas))

E. C. BONARD, J. JORNOD, and A. F. MULLER. *Revue française d'études cliniques et biologiques* [*Rev. franç. Ét. clin. biol.*] **2**, 262–289, March, 1957. 1 fig., bibliography.

From the University Clinic, Geneva, comes this clinical account of 13 cases of disseminated lupus erythematosus, 12 of which were in women. The prominent symptoms, in descending order of frequency, were fever, joint pains, pleurodynia and myalgia, loss of weight, and asthenia. The parts most commonly and most severly involved were the joints (10 cases), followed by the skin; the kidneys were the site of the presenting symptoms in only 2 cases and the heart in one. Poor resistance to infection was noted and was attributed to an abnormal plasma globulin pattern. The authors suggest that lupus erythematosus should be considered in the differential diagnosis of every case of pyrexia of uncertain origin, without waiting for a complete clinical picture to emerge. The multiplicity of the cutaneous manifestations is stressed and the inadequacy of the term " lupus " discussed.

In contrast to the variability of the clinical picture the disease, as a biological syndrome, is remarkably constant. It is characterized by a dysglobulinaemia with excess of globulins (usually of γ globulin and/or of α_2 globulin), and hypo-albuminaemia. The dysglobulinaemia is responsible for a number of abnormal laboratory findings, such as the raised erythrocyte sedimentation rate, abnormal plasma protein electrophoretic pattern, abnormal colloidal (" turbidity ") test results, and false positive reactions in the Widal test and serological tests for syphilis. Among the abnormal globulins there may be a number of antibodies giving rise to haemolysis, leucopenia, thrombocytopenia, a positive reaction to the Coombs test, and most important diagnostically, antinuclear bodies responsible for the appearance of L.E. cells. In all of the 13 cases described the presence of L.E. cells was demonstrated. *A. Swan*

719. **Agglutination of Sensitized Sheep Erythrocytes in Disseminated Lupus Erythematosus**

N. SVARTZ and K. SCHLOSSMAN. *Annals of the Rheumatic Diseases* (*Ann. rheum. Dis.*) **16**, 73–75, March, 1957. 9 refs.

This paper from Karolinska Sjukhuset, Stockholm, reports the results of the examination of serum from 64 cases of disseminated lupus erythematosus, in which the clinical diagnosis had been confirmed by the subsequent course of the disease, by two haemagglutination techniques: (1) that with whole serum in which the heterophile haemagglutinins were adsorbed and removed by normal unsensitized sheep erythrocytes (Ball's modification of the Waaler–Rose technique), and (2) the cold-precipitate technique of the present authors (*Acta med. scand.*, 1953, **146**, 313). In 32 of the 64 cases a positive haemagglutination reaction was obtained with whole serum. In 30 of these 32 cases haemagglutination with whole serum occurred at titres ranging from 1:16 to 1:1,024, while with the cold-precipitate technique only one gave a positive result, the titre in all the rest never rising above 1:8. The single case which gave agglutination with whole serum to a titre of 1:1,024 gave no agglutination with the cold-precipitate fraction. It has previously been demonstrated that in rheumatoid disease the cold-precipitate fraction gives results closely parallel with those obtained from whole serum. The cold-precipitate technique therefore provides a serological means of differentiating between rheumatoid disease and disseminated lupus erythematosus. *Harry Coke*

720. **Urinary Excretion of Creatine and Creatinine in Dermatomyositis**

H. B. CHRISTIANSON, P. A. O'LEARY, and M. H. POWER. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **27**, 431–441, Dec., 1956 [received April, 1957]. 1 fig., 19 refs.

A study is reported from the Mayo Clinic of the urinary excretion of creatine and creatinine of 134 patients with dermatomyositis and 27 patients suffering from other diseases. Increased excretion of creatine was observed in dermatomyositis, as well as in many other diseases, especially those characterized by muscular degeneration and wasting. Creatinuria is especially marked during the acute febrile stage of dermatomyositis. Remission of the disease, whether spontaneous or induced by administration of steroids, is accompanied by creatine. On the other hand, excretion of creatinine is reduced in all phases of dermatomyositis and in other diseases characterized by muscular degeneration.

The authors consider that the urinary excretion of creatine and creatinine is of limited value in the diagnosis and prognosis of dermatomyositis. *A. Swan*

Physical Medicine

721. **Basic Teaching–Training Principles for the Patient with Cerebral Palsy**
H. E. HIPPS. *British Journal of Physical Medicine* [*Brit. J. phys. Med.*] **20**, 34–39, Feb., 1957. 4 refs.

At one time patients with cerebral palsy were treated by " physical therapists " who learnt their methods by trial and error, some methods being good and others useless. When, however, children with cerebral palsy in the United States were assigned to the care of school teachers excellent results were obtained, and this, the present author claims, was because the teachers had been trained to teach. He goes on to elaborate his theme, that the fundamental concepts of teaching and training are just as applicable to the teaching of spastics as to the teaching of normal children; the latter learn by imitation, trial and error, repetition of effort, and sometimes by reason or insight, and the child with cerebral palsy should do the same. Spastic children must learn by doing, and the tedious training in how to relax should be abandoned in favour of learning by imitation and trial and error. They should be taught either individually or in small groups of 3 or 4, larger groups being less satisfactory.

A normal child first learns to hold his head up, then to sit up, then to stand, and then to walk. These are the natural stages of maturation, and they should be the stages in the training of the spastic child. He should be taught only one activity at a time, and must not be confused by attempts to teach him several things rapidly. Constant and prolonged repetition is necessary, because the spastic child learns very slowly. Reward and praise should immediately follow successful achievement. A motive for learning must be introduced, so that the training will make sense to the child. Finally, it must not be forgotten that mental development must proceed at the same time and be equally encouraged.

W. Tegner

722. **Effect of Physiotherapy on Postoperative Pulmonary Complications. A Clinical and Roentgenographic Study of 200 Cases.** [In English]
O. WIKLANDER and U. NORLIN. *Acta chirurgica Scandinavica* [*Acta chir. scand.*] **112**, 246–254, March 28, 1957. 7 refs.

The effect of physiotherapy on pulmonary complications following upper abdominal surgery was studied at Karolinska Institutet, Stockholm, in 200 patients selected at random. The patients were divided into two groups of 100 patients each, Group 1 receiving physiotherapy and Group 2 serving as controls. Group 1 were given breathing exercises and postural drainage twice daily, starting a day or so before operation and continuing until no sputum was obtained. Patients in both groups were given a water-soluble guaiacol–glycerin ether (" resyl ") to decrease the viscosity of bronchial secretions, and were allowed up early. Radiological examination of the lungs were carried out on both groups before operation, on the evening after operation, and on the first and third postoperative days. Pulmonary lesions were divided into three groups according to severity, and the results of treatment were assessed on the changes in these lesions and statistically analysed.

It was found that pulmonary lesions occurred in 59 patients in Group 1 and 77 in Group 2. When minimal changes were ignored there were 13 patients in Group 1 and 24 in Group 2 with atelectasis. In most cases the changes in the lung appeared within a few hours of operation. The incidence of postoperative pulmonary complications rose significantly with advancing age and increased weight, but smoking was not found to be deleterious. The patients in the control group were in hospital for a shorter time than those in the treated group.

J. B. Millard

723. **Observations on the Electrophoresis of Nicotinic Acid.** (Наблюдения над электрофорезом никотиновой кислоты)
V. M. SHPAK, R. I. KARSHENBAUM, and M. F. LYAKSUTKINA. *Вопросы Курортологии, Физиотерапии, и лечебной физической Культуры* [*Vop. Kurort. Fizioter.*] 34–36, No. 2, March–April, 1957. 2 figs.

During a study of reflex responses to various chemical stimuli reactions to the cutaneous electrophoresis of nicotinic acid attracted the authors' attention. The vascular reaction to this drug exhibited a " wave " phenomenon—that is, after a stage of initial hyperaemia, which rapidly faded on switching off the current, there was a second wave of hyperaemia which developed spontaneously 1 to 5 minutes later and was greater in intensity and duration than the first.

The authors claim [without giving statistical details] that cutaneous electrophoresis of nicotinic acid may be usefully employed in the treatment of essential hypertension, and give detailed accounts of 2 successful cases in which a complete, albeit temporary, return of the blood pressure to normal was achieved. After the patient's abdomen had been warmed with a " solux " lamp for 5 minutes, a cathode (12 cm. × 8 cm.) was applied to the supra-umbilical region over a gauze pad moistened with a 0·5% solution of nicotinic acid in distilled water. The anode was applied to the patient's back in the region of D7 or 8. The current (8 to 12 mA) was maintained for two periods of 10 minutes each, with a 5-minute interval between. The course consisted of up to 30 applications at intervals of one or 2 days. Reduction in blood pressure was noted after 8 to 12 applications. The duration of the effect on cessation of treatment varied from 10 days to one year.

A. Swan

Neurology and Neurosurgery

724. **Behçet's Syndrome with Neurological Complications**

N. WADIA and E. WILLIAMS. *Brain* [*Brain*] **80**, 59–71, March, 1957. 2 figs., 31 refs.

Behçet's syndrome is a rare disorder characterized by oral and genital ulceration and hypopion iritis. Recurrent attacks tend to occur 3 or 4 times a year and the mouth, genitalia, and eyes may be affected separately or together. Ocular involvement is at first unilateral, but later there may be serious disturbances of vision in both eyes, often with extreme pain and sometimes blindness. Skin lesions are common, including erythema nodosum and pyoderma. Involvement of the central nervous system is rare, but has resulted in the death of the patient on at least 3 occasions. Such central nervous involvement has been recorded in the literature in 10 cases, and 3 additional cases are now described from the London Hospital. The involvement is widespread and may include meningitis, spastic weakness of the limbs, external ophthalmoplegia, acute confusional states, and progressive dementia, with varying changes in the spinal fluid. The precise aetiology is still obscure. There is some evidence that cortisone is of value in treatment, especially in the early stages, but reports of its effects are somewhat conflicting. *Hugh Garland*

725. **Vascular Mechanisms of Birth Injury**

R. M. NORMAN, H. URICH, and W. H. MCMENEMEY. *Brain* [*Brain*] **80**, 49–58, March, 1957. 9 figs., 26 refs.

While stagnant anoxia due to venous engorgement has come to be regarded as the most important pathogenetic mechanism of cerebral birth injury, the present authors suggest that the importance of the arterial system in the causation of such injuries has probably been underestimated. In support of this thesis they describe 2 cases, one that of a male imbecile who died at 28 months and the other that of a mentally defective female who died at 10 months, in each of which there was reason on clinical grounds to suspect cerebral birth trauma. Histological studies showed scattered areas of cortical atrophy in the cerebrum and cerebellum of both brains; these occupied either the boundary zone between two main arterial territories or lay within the field of supply of individual arteries. It is thought that the boundary-zone lesions probably resulted from a fall of the systemic blood pressure below the critical level as a result of shock associated with trauma. The second type of lesion is thought to have resulted from compression of arteries at certain preferential sites; for example herniation of the uncus at birth may compress the anterior choroidal artery and branches of the posterior cerebral artery against the edge of the tentorium; such compression would result from displacement of brain substance during the process of birth and would be facilitated by coincidental reduction of the blood pressure. In the second case there were also paraventricular softenings of the central white matter and changes in the basal gangiia attributable to obstruction of the great vein of Galen. *Hugh Garland*

726. **Hemichorea (Hemiballismus) without Lesions in the Corpus Luysii**

J. P. MARTIN. *Brain* [*Brain*] **80**, 1–10, March 1957. 5 figs., 13 refs.

The association of hemichorea with lesions of the corpus Luysii (subthalamic nucleus) of the opposite side has been recognized for some years on the basis both of clinico-pathological study and of experiments on monkeys. Occasionally, however, the corpus Luysii has been found to be undamaged post mortem in patients who had suffered from hemichorea. In animal experiments Mettler and his associates have already established that hemichorea can be abolished by destruction of the globus pallidus or its efferent fibres and it has been inferred that the occurrence of movements resulting from loss of the influence normally exercised by the corpus Luysii on the pallidum may result from interruption of fibres connecting the subthalamic nucleus with the globus pallidus, the two structures being connected by a "to-and-fro" fibre system. In the present paper from the National Hospital, Queen Square, London, a description is given, together with pathological studies, of 3 cases of hemichorea in which the findings supported this view, the relevant corpus Luysii being intact in each case [though perhaps the third case is not totally convincing and has required a certain amount of special pleading].

[The terms hemichorea and hemiballismus are used synonymously in this paper. If the two words have precisely the same meaning, then one of them is redundant, but it is questionable whether the frequently violent unilateral movements to which most neurologists apply the term hemiballismus differ only in quantity from those of so-called rheumatic hemichorea. It would seem that either the two terms should not be regarded as synonymous or else, as is not infrequent in neurology, the terminology is inadequate.] *Hugh Garland*

727. **Hypertrophic Osteosclerosis (Bony Spur) of the Lumbar Spine Producing the Syndrome of Protruded Intervertebral Disk with Sciatic Pain**

M. T. SCHNITKER and F. C. CURTZWILER. *Journal of Neurosurgery* [*J. Neurosurg.*] **14**, 121–128, March, 1957. 3 figs., 14 refs.

Among a series of 154 patients operated on at St. Vincent's Hospital, Toledo, Ohio, for symptoms of prolapsed lumbar intervertebral disk (that is, backache and unilateral sciatica) 9 were found to have instead a bony spur (localized hypertrophic osteosclerosis) which was compressing a nerve root. Of these 9 patients 8 were females and only one male, contrasting with a 2:1 male

preponderance in cases of ordinary prolapsed disk. In 7 of the cases the symptoms were precipitated by a fall on the buttocks, and it is postulated that a fracture or a periosteal tear at the interarticular isthmus with subsequent new bone formation may be an important factor in the aetiology. Pain was not as severe in onset as usually occurs in true herniation of a disk; the duration of symptoms was from 2 to 12 months. In 4 cases the patient complained of numbness in the involved extremity and 2 had paraesthesiae. Coughing and straining exacerbated the symptoms in 4 cases. Relief was obtained by 3 patients following rest in bed and temporary relief by another 3, but there was recurrence on mobilization. Physical examination showed no significant differences from the picture of prolapsed disk. Of interest was the fact that in 8 cases the lesion occurred at the L4–L5 articulation, compressing the root of L5, while the remaining case was at L3–L4 involving the L4 nerve root.

Straight *x*-ray examination showed obliquity of the facets of the lateral intervertebral joint at the suspected level, and also a deformity which the authors term a "bulbous facet". The deformity may be verified by lumbar myelography in many instances. All 9 cases were treated by unilateral hemilaminotomy. At operation the bony eburnation was found to arise from the medial margin of the facet or adjacent to the facet, that is, on the interarticular isthmus. Removal of the exostosis relieved the symptoms completely in 8 of the 9 cases. The authors regard the lesion as a manifestation of traumatic arthritis, and comment on the relief of back pain which followed operation in these cases, in contrast to its frequent persistence following operative removal of an intervertebral disk. *J. V. Crawford*

CEREBRAL VASCULAR DISORDERS

728. **Carotid Compression in the Neck. Results and Significance in Carotid Ligation**

E. S. GURDJIAN, J. E. WEBSTER, F. A. MARTIN, and W. G. HARDY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 1030–1036, March 23, 1957. 6 figs., 18 refs.

In this paper from the Wayne University Neurological Surgery Service, Detroit, the authors describe their experience of carotid artery ligation electively performed for intracranial vascular lesions in 63 patients, the common carotid being ligated in 60 and the internal carotid in 3. In each case digital compression of the artery in the neck was first carried out in an attempt to determine whether ligation would be tolerated. In some patients, however, compression or even palpation of the vessel caused bradycardia, hypotension and syncope due to stimulation of the carotid sinus, and these patients were therefore given atropine. The pattern of the electrocardiogram and blood-pressure recordings were used to identify these vagal effects. If the patient was able to stand carotid compression for 10 minutes, it was assumed that the collateral circulation was sufficient to permit ligation without complications. In 2 cases a ligation was thought advisable but was not carried out because of the untoward effects of the compression tests. There were 3 deaths which could not be attributed directly to the ligation, and 4 cases of hemiparesis which was short-lasting in 3. *R. G. Rushworth*

729. **Carotid Thrombosis. An Evaluation and Follow-up Study of 65 Cases.** [In English]

K. SASTRASIN. *Acta neurochirurgica* [*Acta neurochir. (Wien)*] **5**, 11–37, 1957. 24 figs., bibliography.

The author presents from the University of Zürich an analysis and detailed evaluation of 65 cases of thrombosis of the carotid artery collected between 1938 and 1955. In all cases the lesion was demonstrated by arteriography, or after surgical removal, or at necropsy. Of the 65 patients, of whom 51 were male and 14 female, most of them in the 5th and 6th decade, 60 were suffering from hemiparesis which in 20 cases was severe, the upper limb and face being the worst affected. Sensory disturbance was present in 20, and dysphasia in 34, being a motor dysphasia in about half of these and combined motor and sensory dysphasia in the other half. Some 50% of the patients complained of headache on the side of the lesion, 24 showed definite psychological disturbance, 19 had visual disturbances (in most cases hemianopia), while 2 were suffering from optic atrophy on the side of the lesion.

Left-sided thrombosis seemed to be nearly twice as common as a right-sided lesion. In 40 cases the occlusion was just above the bifurcation of the common carotid, while in the remainder it was higher up in the internal carotid. The blood pressure in 17 of the patients was above 150/90 mm. Hg; in all cases the Wassermann and Kahn reactions were negative. The aetiology was surprising in that out of the 27 cases treated by resection and 6 examined at necropsy 19 showed thromboangiitis obliterans (Buerger's disease) while 8 showed evidence of arteriosclerosis; in the others the changes were non-specific. Of the 50 patients followed up 22 had died, while of the 28 still living only 12 were able to work. It did not appear that the course of the disease was affected by surgical treatment. *G. S. Crockett*

730. **Aneurysms Arising at the Internal Carotid–Posterior Communicating Artery Junction**

P. HARRIS and G. B. UDVARHELYI. *Journal of Neurosurgery* [*J. Neurosurg.*] **14**, 180–191, March, 1957. 6 figs., 20 refs.

A common site for intracranial aneurysms is at the point where the posterior communicating artery takes origin from the internal carotid artery. In the series here reported from the Royal Infirmary, Edinburgh, this was the site in 90 (27%) out of a total of 326 intracranial aneurysms. The commonest symptom (75 cases) was subarachnoid haemorrhage, which in 29 was the only symptom. In 34 cases it was recurrent, usually at about the 10th day. Palsy of the third cranial (oculomotor) nerve was present in 40 patients, and contralateral hemiparesis in 26; in 2 of the latter a temporal lobe haematoma was demonstrated by angiography while arterial spasm is postulated as the cause of the hemiparesis in

the others. Ipsilateral frontal and orbital pain were initial symptoms in 12 patients; it was noted that in most of these cases compression of the carotid artery in the neck abolished the pain temporarily. Angiography is necessary to confirm diagnosis, to establish the anatomy of the aneurysm, to outline any other aneurysms which may be present, and to demonstrate the adequacy of the anastomotic circulation. The authors prefer to perform this investigation as soon as possible, but in very ill patients careful timing is required and prolonged unconsciousness, severe mental confusion, and marked abnormalities of blood pressure are given as reasons for delaying the procedure, which is carried out under general anaesthesia after premedication with papaverine and infiltration of the carotid sheath with a local analgesic. The risks of angiography in the presence of recent subarachnoid haemorrhage are discussed.

While the best mode of treatment depends on the features of each individual case the authors have employed mainly two methods, namely, proximal ligation of the carotid artery in the neck (66 cases) or direct surgical obliteration of the aneurysm (12 cases); the remaining patients were considered to be too ill for surgical treatment. The former method is preferred, but the authors suggest direct obliteration is indicated if (1) tests show there is inadequate anastomotic circulation; (2) the aneurysm fills during the test of contralateral anastomotic circulation; or (3) trial occlusion of the carotid results in neurological changes. In the present series there were 7 deaths following proximal carotid ligation, one case of recurrent haemorrhage, 17 of hemiparesis (transient in 12), while 5 patients showed psychic changes and 4 developed epilepsy. Among the 12 patients treated by obliteration of the aneurysm there were no deaths, but one patient suffered recurrent haemorrhage, 3 developed hemiplegia, and 3 showed psychic changes and epilepsy. Thus of the 66 patients treated by carotid ligation 35 (53%) did well, while of the 12 patients treated by direct attack 6 (50%) had no complications. The importance of clinical and angiographic follow-up in these cases is emphasized. *J. V. Crawford*

731. **Hypertensive Strokes**

A. W. D. Leishman. *Lancet* [*Lancet*] **1**, 437–441, March 2, 1957. 3 figs., 11 refs.

A group of 234 hypertensive patients under regular observation since 1946 provided an opportunity of studying the natural history of hypertensive strokes. None of the group (95 men and 139 women) was over 60 years of age at the time of the initial examination, and none had received effective treatment for hypertension. The blood pressure was recorded as the average of readings in both arms, in lying and standing positions. Hypertension was diagnosed when the diastolic pressure exceeded 100 mm. Hg. During the 10 years covered by the study 97 (41%) of the patients died, the commonest cause being stroke (41 cases). This report is confined to the 56 patients who had a stroke before the age of 60, the 31 fatal cases forming Group 1 and the 25 non-fatal cases Group 2. As controls (Group 3) the author chose 32 patients with a diastolic pressure of not less than 130 mm. Hg, who had not experienced a stroke during " an average of 7 years beyond the average age at which strokes developed in the first two groups ".

Post-mortem examination was not performed in any of the fatal cases but the author considers that with very few exceptions the fatal strokes were due to cerebral haemorrhage and the non-fatal to cerebral thrombosis. In Group 1 as compared with Group 3 there were more patients with an excessively high blood pressure (diastolic 150 mm. Hg or more), with signs of renal damage but not an excessively high blood pressure, and with a history of previous strokes. Group 2 included only slightly more patients with excessively high blood pressure than Group 3, but four times as many with a family history of strokes. Retinal haemorrhages and exudates were a little more frequent in Groups 1 and 2 than in Group 3. The incidence of transient cerebral episodes was about the same in all three groups; this is considered to support the view that cerebral arterial spasm is the cause of " little strokes ", and not thrombosis.

It is concluded that: (1) there are no features permitting prediction of cerebral thrombosis in a hypertensive patient; (2) cerebral haemorrhage cannot be related either to the severity or to the character of the hypertensive condition, and is, therefore, not predictable; and (3) since cerebral haemorrhage is probably due to fibrinoid necrosis, which is a reversible condition, the incidence of the latter should be considerably reduced by effective hypotensive treatment.

[This is an important paper which should be read by all concerned in the management of hypertensive patients.] *P. D. Bedford*

EPILEPSY

732. **The " March " of Temporal Lobe Epilepsy**

J. R. Stevens. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **77**, 227–236, March, 1957. 18 refs.

In this paper from the University of Oregon Medical School, Portland, the author attempts, by analysing the sequence of events in temporal lobe seizures, to determine whether there is a characteristic "march" of symptoms and signs in epileptic attacks of this sort. In all, 40 such patients were examined and information regarding the attacks was elicited under medication with sodium amytal, descriptions of motor manifestations during the attack being obtained from reliable observers; none of the patients had any evidence of cerebral neoplasm or progressive degenerative disease. In 37 cases the electroencephalogram (EEG) showed abnormalities in the temporal or basal regions of the brain, but in the other 3 the EEG was consistently normal.

Certain patterns in the organization of seizures emerged from the analysis and demonstrated a strong interrelationship between somatic and visceral sensation and emotional states. The commonest pattern consisted in a grouping of epigastric aura with a feeling of fear and danger accompanied by concomitant motor activity of the "flight–fight" pattern. Only a few patients, namely those with a cephalic aura, experienced pleasant anticipa-

tory feelings free from fear. In 7 cases the patient had an aura of vertigo or tinnitus and in 5 of these it was followed by an illusory state, only one patient experiencing fear. Olfactory hallucinations of a disagreeable sort were never the first symptom of an attack, this being in contrast to pleasant odours which, when present, were always the first symptom and were followed by intense mental confusion, without however fear or flight–fight manifestations. The author suggests that further study of temporal lobe attacks may lead to greater understanding of the organization of the temporal lobe and the part it plays in emotional feeling and expression. *J. B. Stanton*

733. **Meprobamate Therapy for Convulsive Disorders of Children**

F. J. AYD. *Bulletin of the School of Medicine University of Maryland* [*Bull. Sch. Med. Maryland*] **42**, 2–5, Jan., 1957. 3 refs.

Since meprobamate has been shown to have a potent anticonvulsant action in animals, it was given a clinical trial for one year in 25 children, aged 6 to 15 years, whose epileptic seizures had proved refractory to other anticonvulsant drugs. It was found that meprobamate was not only ineffective against grand mal epilepsy, but might aggravate the attacks. The drug was effective, however, in 7 out of 10 children with petit mal and 4 out of 5 with myoclonic epilepsy. Drowsiness was the most common side-effect, and one patient had a severe generalized dermatitis. Tremor was observed in one patient and incoordination in 3 patients. The average daily dose ranged from 1·6 to 4 g. It is concluded that meprobamate has some advantages over other drugs for the minor convulsive disorders of children. *J. Foley*

734. **Phenacemide in the Treatment of Epilepsy. Results of Treatment of 411 Patients and Review of the Literature**

S. LIVINGSTON and L. L. PAULI. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 588–592, March 28, 1957. 31 refs.

At Johns Hopkins Hospital, Baltimore, a series of 411 patients suffering from epileptic seizures of various types were treated with phenacemide (phenylacetylurea). Anti-convulsant treatment had been given to 303 of these for at least 6 months previously, and to 157 of this group in whom the seizures were partially controlled phenacemide was given in addition to other drugs; in the remaining 146, previous medication which had been ineffective was gradually withdrawn and replaced by phenacemide only. Only 89 of the 411 patients were over 15 years of age; the age of the youngest was 2½ years. The dosage of phenacemide was 250 to 500 mg. twice daily for children under 3 years and 500 to 1,250 mg. four times daily for adults.

The drug was effective only in patients suffering from psychomotor seizures; these were completely controlled in 12 out of 28 patients not previously treated, in 16 out of 54 in whom attacks had been partially controlled, and in 7 out of 43 refractory to previous treatment. A most undesirable side-effect was a personality change which occurred in 61 (15%) of the patients in the series, the affected patients becoming restless, irritable, destructive, and belligerent. Suicidal tendencies were observed in 54 and the drug had to be discontinued. Hepatitis occurred in 5 cases but cleared up after withdrawal of the drug. Skin rashes were noted in 12 cases, and these too cleared up when phenacemide was discontinued. Although other toxic effects, including aplastic anaemia, had been reported, the present authors have not encountered such toxic reactions in this series. They consider that the drug has a place in the treatment of psychomotor epilepsy. *William Hughes*

735. **Chlorpromazine (Thorazine) Treatment of Disturbed Epileptic Patients**

V. I. BONAFEDE. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **77**, 243–246, March, 1957. 1 ref.

In continuation of a previous study (*A.M.A. Arch. Neurol. Psychiat.*, 1955, **74**, 158; *Abstracts of World Medicine*, 1956, **19**, 240) the author now reports the results in 165 epileptic patients who were treated at Craig Colony, New York State, with chlorpromazine over a period of 2 to 12 months for behavioural and emotional disturbances. Two-thirds of these patients suffered from idiopathic epilepsy and the remainder from symptomatic fits and the majority were mentally defective; their ages ranged from 3 to 69 years and most of them were female. Chlorpromazine was given daily in doses of 50 to 600 mg., but in most cases the maintenance dose was between 200 and 400 mg. daily, only a few receiving 600 mg. daily. Anticonvulsant drugs were continued and in some cases their dosage had to be increased. Improvement in behaviour was assessed by ward physicians and nursing staff.

Of the 165 patients 45% showed marked improvement, 39% slight to moderate improvement, and 16% no change. All but 2 of the 19 children in the series showed significant behaviour improvement. In 10% of the patients there was a marked increase in frequency of the seizures when the administration of chlorpromazine was accompanied by a simultaneous reduction in the usual doses of barbiturates; on the other hand 25% showed an appreciable reduction in frequency of fits under chlorpromazine medication. The majority of patients steadily gained weight during treatment and complications were rare. No clinical evidence of toxic effects due to a barbiturate-potentiating effect of chlorpromazine on the former drugs was seen. The author concludes that chlorpromazine is a valuable drug in the treatment of emotionally disturbed epileptics.

J. B. Stanton

736. **Experimental and Clinical Results Obtained with Certain Recently Introduced Anticonvulsants.** (Résultats expérimentaux et cliniques obtenus au moyen de quelques substances anti-épileptiques récentes)

L. SOREL. *Confinia neurologica* [*Confin. neurol.* (*Basel*)] **17**, 16–42, 1957. 11 figs., 15 refs.

Writing from the Neurological Institute, University of Louvain, the author describes an evaluation of a number of anticonvulsant drugs. The first half of the paper is devoted to a description of animal experiments which

consisted in determining the protective effect of each drug on the electroencephalogram (EEG) of the rabbit after the animal had received a standard intravenous dose of "cardiazol" (leptazol), "phenergan" (promethazine hydrochloride), or amethocaine, which normally cause EEG dysrhythmia. The drugs were administered by mouth in "infratoxic" doses, defined as the highest dose which when administered to an aliquot number of animals produces none of the clinical signs of toxicity in any. (Incidentally, the author points out that the "infratoxic" dose in mg. per kg. body weight for the rabbit corresponds to the average dose in mg. which can be given three times daily to adult human subjects without causing toxic side-effects.) The results of these investigations for 10 different drugs are given in tabular form.

The author then goes on to describe clinical trials carried out with "doriden" (glutethimide), "gemonil", "hydrane", "milontin" (phensuximide) "mysoline" (primidone), and "trinuride" (phenylethylacetylurea) on epileptic patients who had proved largely or totally resistant to other anticonvulsant drugs; the periods of observation ranged from 2 months to 3 years. The author discards the first four drugs mentioned above for any but exceptional use, on the grounds of unsatisfactory results and potential toxicity. Primidone and trinuride he considers worthy of retention, regarding the latter as the greatest advance in anticonvulsant therapy in the last 4 years. This substance is virtually non-toxic and, when combined with barbiturates and hydantoinates, completely suppresses attacks in about 25% of patients; it is particularly the drug of choice for patients with temporal lobe epilepsy. He points out that the comparatively low dosage of nydrane and phensuximide used in this study may explain the lack of benefit obtained with these substances. *J. B. Stanton*

737. **Diamox (Acetazolamide) in the Treatment of Epilepsy**
T. WADA, T. SATO, and S. MORITA. *Diseases of the Nervous System* [*Dis. nerv. Syst.*] **18**, 110–117, March, 1957. 1 fig., 9 refs.

PERIPHERAL NERVES

738. **Compression of Median Nerve in Carpal Tunnel and Its Relation to Acroparaesthesiae**
H. GARLAND, J. P. P. BRADSHAW, and J. M. P. CLARK. *British Medical Journal* [*Brit. med. J.*] **1**, 730–734, March 30, 1957. 1 fig., 9 refs.

The authors report their clinical and operative experience at the General Infirmary at Leeds in 53 cases of acroparaesthesiae. The patients complained of attacks of pain and paraesthesiae in the digits and palm of one or both hands, with no neurological deficit in some cases, and with varying degrees of motor and sensory disturbance distal to the wrist in others. The onset of symptoms was in the fifth and sixth decades in about one-half, with smaller peak at 25 to 30 years. Predisposing causes included increased domestic activity in 38 women, change of occupation in 4 men, fall on the wrist in 3 cases, and pregnancy in 2. Gross arthropathy of the wrist was found in 3 and changes typical of rheumatoid arthritis in one case out of 8 in which radiography was performed. In all except 8 cases there were varying degrees of weakness and wasting of the thenar muscles and impairment of cutaneous sensibility. Of 6 patients investigated by electromyography, evidence of denervation of muscles supplied by the median nerve below the wrist was found in 4. Pressure on the volar aspect of the wrist provoked an attack in 3 patients. Eight patients were tested by cuff occlusion of the brachial artery (at 220 mm. Hg) before operation and the remainder during follow-up. In 6 of the 8 preoperative tests pain, paraesthesiae, and sensory impairment developed in the median-nerve distribution in the hand and digits within 2 minutes of occlusion.

The technique and results of operative treatment by exposure and division of the transverse carpal ligament are described. No patient was made worse by the operation, and the only operative complication was swelling and pain at the site of operation, which occurred in half the cases and persisted for some weeks. In all, 53 operations were performed on 35 patients. In 29 of these no abnormality was seen in the median nerve. In 20 the nerve was seen to be swollen proximal to the ligament for a distance of 1 to 3 inches (2·5 to 7·5 cm.), and in many cases this swelling subsided within a few minutes of division of the ligament. In 11 cases the nerve was clearly flattened beneath the ligament, and in 3 this flattening was seen to disappear during the operation. A follow-up was conducted on 33 of the 35 patients for periods of 2 months to 7 years. Of 18 patients who had undergone bilateral operation, 10 had complete relief on both sides, 3 relief on one side and slight residual symptoms on the other, and 3 continued to have attacks (but in one case these were probably related to cervical spondylosis). Of 17 patients who had had a unilateral operation, 11 were symptom-free and the remainder greatly improved. Before operation 19 patients had sensory impairment and 29 weakness (10 with muscle wasting). At follow-up examination only 2 cases were found with sensory impairment and 3 with moderate weakness.

In the remaining 18 cases rest and avoidance of work or movements which precipitated attacks were advised, and 17 of these patients were followed up for periods of one month to 6 years. Of 8 patients with bilateral symptoms, 3 were relieved, though the symptoms recurred when the regimen was stopped, 1 was slightly improved, and 4 derived no benefit. Of 9 unilateral cases, symptomatic relief related to the regimen was seen in 5. Sensory loss was present in 8 cases and was restored in 5, whereas in 3 cases sensation deteriorated during treatment. Of 7 cases with muscle wasting, recovery was noted in 3 and deterioration in 4.

The authors conclude that on the evidence submitted the clinical condition is due to compression of the median nerve in the carpal tunnel. They state that after surgery there was invariable and dramatic relief of symptoms, which was maintained, and improvement or complete recovery in the neurological deficit, and that this must therefore be regarded as the treatment of choice.
Brodie Hughes

Psychiatry

739. **Homosexuality: an Analysis of 100 Male Cases Seen in Private Practice**
D. CURRAN and D. PARR. *British Medical Journal* [*Brit. med. J.*] **1**, 797–801, April 6, 1957. 9 refs.

In a series of 5,000 cases seen in private psychiatric practice those patients in whom homosexuality was the presenting problem or a major part of the diagnostic formulation constituted 5% of all males and 0·3% of all females over the age of 16. Of the 100 such cases in males here studied (chosen on the basis of adequate documentation and not regarded as representative) about half showed other psychiatric abnormalities, usually slight. The social status of the group as a whole was high. Except for the distinction between paedophiliacs and adult seekers, the condition was variable within individuals. On classification according to a scale roughly equivalent to the Kinsey rating scale no differences in social or economic success, stability, or social worth were found between the practising and the continent groups or between those admitting to buggery and the other practising homosexuals. The 17 paedophiliacs showed certain statistically significant differences and tended to be more socially isolated than the others.

So far as it goes, the authors' analysis of their material supports the view (held by Freud and by Kinsey) that the main psychosexual pattern is established not later than puberty, though some changes were found in a few of the cases followed up. No statistically significant differences in results were found between 25 patients treated by psychotherapy of various kinds and a matched untreated group, though some of the treated group appeared to come to better terms with their problems at a subjective level. *J. L. Standen*

740. **Intrathecal Administration of Hyaluronidase: Effects upon the Behavior of Patients Suffering from Senile and Arteriosclerotic Behavior Disorders**
D. E. CAMERON, L. LEVY, and W. HUNZINGER. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **113**, 893–900, April, 1957. 5 figs., 22 refs.

741. **Rauwiloid Therapy in Alcoholism**
J. THIMANN, F. G. BUCKNAM, J. W. GAUTHIER, and T. A. O'CONNELL. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **113**, 694–697, Feb., 1957. 8 refs.

At the Washington Hospital, Boston, "rauwiloid" was tried as a tranquillizing agent in sub-acute and chronic alcoholism in 199 patients, all except 7 being alcohol addicts. The double-blind method was used, 50 patients receiving rauwiloid in a dosage of 2 to 4 mg. twice or three times a day and the others receiving two different relaxant drugs structurally related to mephenesin, or a placebo. Administration of the drugs in the sub-acute stage of intoxication was started 1 to 2 days after admission to hospital and in the acute alcoholic psychoses after termination of the acute phase. Treatment was continued into the chronic stage of alcoholism whenever indicated. In 40 of the 50 patients given rauwiloid some improvement was noted; in the two groups receiving the relaxant drugs the results were similar, but in the group given a placebo they were much inferior. Administration of the drugs was supplemented in all cases by psychotherapy.

The authors consider that rauwiloid "proved effective for the psychogenic factors of chronic alcoholism", and that the use of this drug for the treatment of alcoholism merits further investigation. *John A. Clark*

742. **A Clinical Evaluation of Meprobomate Therapy in a Chronic Schizophrenic Population**
K. TUCKER and H. WILENSKY. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **113**, 698–703, Feb., 1957. 7 refs.

An investigation is reported of the value of meprobamate in relieving the anxiety and tension seen in 63 male schizophrenic patients at the Franklin Delano Roosevelt Veterans Administration Hospital, Montrose, N.Y. All the patients had been ill for at least 18 months. The investigation was conducted over a period of 18 weeks—an observation period of 2 weeks being followed by a treatment period of 12 weeks during which the patients received either the drug or a placebo, and finally a 4-week post-treatment observation period. Meprobamate was given by mouth initially in a dosage of 400 mg. four times a day, rising to a maximum of 1,200 mg. four times a day. A double blind method of control was used. The results were assessed at psychiatric interviews at 4-week intervals, at weekly ward conferences with the nursing staff, and from the replies to a psychological questionary of 74 "anxiety" items on three separate occasions.

It was found that in 13 of the 32 patients receiving meprobamate there was a significant improvement compared with 3 of 31 patients receiving the placebo. It is concluded that meprobamate is clearly of value in reducing the anxiety and tension level of patients suffering from chronic schizophrenia. *John A. Clark*

743. **The Treatment of Depressive States with Haematoporphyrin (Nencki).** (Behandlung von Depressionszuständen mit Hämatoporphyrin-Nencki)
O. BRÜEL. *Psychiatria et Neurologia* [*Psychiat. Neurol. (Basel)*] **133**, 1–17, Jan.–Feb., 1957. 43 refs.

The author describes the results obtained in private practice in Copenhagen with haematoporphyrin in the treatment of 220 ambulatory patients who suffered from depressive illnesses for which systematic psychotherapy was not indicated, and who wished to avoid admission to hospital. In mild cases oral medication was given, the dosage fluctuating between 10 and 30 drops three

times daily before meals. In moderately severe cases a course of 10 intramuscular injections each of 1 ml. (2 mg.) every second day was given, followed after a fortnight's interval by another course of 10 injections of 2 ml. (4 mg.) every second day. In severe cases the oral and parenteral treatment was combined. The author points out that this treatment is contraindicated in patients with hepatic or renal disease, in those with advanced arteriosclerosis, and in the presence of febrile infections. The medication causes increased photosensitivity of the skin.

Of the 220 patients so treated, who ranged in age from 21 to 72 years and whose duration of illness varied from 6 months to 40 years, 60% were cured, 20% showed some improvement, and 20% remained unchanged. (The author had previously obtained similar results in 100 depressed patients treated up to 1947.) When treatment was successful improvement appeared within 12 days. The best results were obtained in cases of endogenous depression, but the treatment was less successful in involutional melancholia and in cases in which the depression had become "stabilized" and the patients habituated to it; of these last, however, there were only 18 in the present series. *F. K. Taylor*

744. **Psychiatric Uses of Meratran**

A. G. FULLERTON. *Journal of Mental Science* [*J. ment. Sci.*] **102**, 801–804, Oct., 1956. 3 refs.

At Herrison Hospital, Dorchester, 40 chronic psychotic male patients were given 6 mg. of "meratran" (pipradol) daily in three divided doses orally after meals. The investigation was carried out using the "double blind" technique, the patients being divided into two arbitrary groups one of which received the drug and the other a placebo for a period of 4 weeks, when the medication in the two groups was reversed for a further 4 weeks.

The drug caused increased alertness and activity, did not affect blood pressure, pulse rate, or sleep, and an observed decrease in appetite was only temporary. In anxious, agitated, and deluded patients, however, undesirable effects were observed in the form of excessive agitation and increased delusional activities. In the 27 schizophrenic patients in the series the results were disappointing. Some improvement occurred in 5 of the patients, 12 showed no change, and 10 were worse. The 13 patients with depressive symptoms showed a better response, 9 being improved, 3 unchanged, and one, a senile patient with delusions, becoming worse.

F. K. Taylor

745. **The Use of Electroplexy (E.C.T.) in Psychiatric Syndromes Complicating Pregnancy**

S. SMITH. *Journal of Mental Science* [*J. ment. Sci.*] **102**, 796–800, Oct., 1956. 20 refs.

After a brief discussion of the various views for and against the use of electric convulsion therapy (E.C.T.) in pregnancy the author reports the results of such treatment in 15 pregnant women aged 18 to 35 years who were admitted to Barrow Gurney Hospital, Bristol, after such measures as psychotherapy, change of environment, and administration of analeptic drugs had proved ineffective. This number represented 0·47% of all female patients admitted to the hospital during 5 years. The majority of the patients had marked depressive symptoms, and 2 were schizophrenic. In 5 cases a relaxant (suxethonium bromide) was used. E.C.T. was given at any time during pregnancy, being performed in 2 cases before the second month.

No precipitation of labour or any suggestion of miscarriage was noted as a result of the treatment. Prolonged labour occurred in only one case, and this was due to common obstetrical causes. The children born of these pregnancies were followed up for periods of one to 5 years after birth. No intellectual deficiency, physical abnormality, or any other significant anomaly was observed. Neurotic traits occurred in only 2 children, but both of these came from unstable and highly neurotic families. *F. K. Taylor*

746. **Deteriorated Psychotic Patients—Their Treatment and Its Assessment**

A. A. BAKER and J. G. THORPE. *Journal of Mental Science* [*J. ment. Sci.*] **102**, 780–789, Oct., 1956. 1 fig., 9 refs.

The authors state that the evaluation of therapeutic regimens in deteriorated psychotic patients of long standing in mental hospitals suffers from two main handicaps. In the first place, it is difficult to decide which of several factors may have brought about improvement. It is well known, for example, that the mere fact of focusing attention on patients may have a beneficial effect. The second handicap is the unreliability of existing scales for rating improvement in behaviour; these, in the authors' opinion, are either too complex or too subjective in scoring, and they have therefore devised their own rating scale.

This scale has been applied at Banstead Mental Hospital, Surrey, to three groups of deteriorated schizophrenic patients all of whom were under 50 years of age, had been in hospital for at least 5 years, and had not had any active treatment for at least a year. Each group contained 16 patients, randomly selected. Those in the first group were moved to a small and well-staffed ward where they received special attention in the form of habit training and efforts to improve their social behaviour. Those in the second group received electric convulsion therapy (E.C.T.) of up to 20 or more treatments. The third group served as control and remained in their usual ward without any change of routine. The results showed that out of 13 behaviour items on the authors' rating scale 6 could not be reliably or validly measured. Analysis of the other items revealed that the patients in the first group, that is those who received special nursing attention, talked and worked more and their ability to dress themselves improved. In the group given E.C.T. there was a significant reduction of feeding difficulties.

F. K. Taylor

747. **Agranulocytosis in Patients Treated with Thorazine. Report of a Fatal Case**

N. RASKIN. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **113**, 991–992, May, 1957. 3 refs.

Dermatology

748. **The Influence of Irradiation of the Pituitary Gland on Acne**

T. BUTTERWORTH and G. W. CHAMBERLIN. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **75**, 502–508, April, 1957. 8 refs.

In view of accumulated clinical and experimental evidence of the relationship between pituitary secretion and the activity of the sebaceous glands and the evolution of acne, two groups of patients with acne were treated at the Reading Hospital, Reading, Pennsylvania, solely by irradiation of the pituitary gland. *X* rays at 200 kV and 15 mA were used, the technical factors for the two groups being: (1) H.V.L. 0·95 mm. Cu, F.S.D. 54 cm., field size 6 cm. diameter; 100 r (in air) daily to alternate temporal fields for 4 days (23 patients) or 6 days (2 patients); (2) H.V.L. 104 mm. Cu, F.S.D. 50 cm., field size 6×8 cm.; 100 r (in air) weekly to alternate temporal fields for 8 treatments (28 patients). By the first method the pituitary dose was 132 r with 4 and 200 r with 6 treatments. The second method gave a pituitary dose of 33 r at each sitting, and it is estimated that when account is taken of the time–dose factor and other variables the biological effect of the full course of treatment was comparable to that of 4 treatments by the first method.

Treatment was given in the autumn and winter months and assessment of results made 4 to 6 months later. Of the first group, 17 (68%) were considered to be "greatly improved" or "cured", while 3 (12%) showed no obvious change. The results in the second group were slightly poorer, and improvement was also slower in appearing. Of 7 control subjects who received no treatment and were observed over the same period, only one showed any spontaneous improvement. Of the 25 patients in the first group, 23 were re-examined 16 to 18 months after treatment, when 3 were found to have deteriorated, whereas 7 had improved since the first assessment. The only complication worthy of note was a temporary alopecia of the treated sites, appearing 3 weeks after therapy and clearing within 5 months.

Such a form of therapy is not advocated as a routine measure. *Allene Scott*

749. **Pyoderma Gangrenosum. A Clinical Study of Nineteen Cases**

H. O. PERRY and L. A. BRUNSTING. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **75**, 380–386, March, 1957. 2 figs., 9 refs.

In an attempt to define more clearly the entity and course of pyoderma gangrenosum the authors have reviewed the records of 19 cases of this disorder seen at the Mayo Clinic between 1949 and 1954. The aetiology, clinical findings, histopathology, bacteriology, and the results of radiological investigations are described in detail. Where no associated intestinal lesion was demonstrable on proctoscopic examination or by radiography of the large bowel, an *x*-ray examination of the remainder of the gastro-intestinal tract was undertaken. Several of the patients exhibited undue sensitivity to the halogens, but further investigation failed to support the clinical impression that this finding might be a clue to the better understanding of this disease. In 3 cases there were hitherto undescribed vesiculo-bullous eruptions similar to those of dermatitis herpetiformis.

The complications which arose, and the various forms of local antiseptic and non-specific systemic medications used, are described. The authors state that no form of treatment is effective unless the underlying disease process is controlled. They have found that long courses of salicylazosulphapyridine is the most effective of all forms of treatment, the dosage usually employed being 0·5 g. every 3 hours for seven or eight doses during a 24-hour period. For maintained therapy it is suggested that the drug be taken for 10 days, alternating with a 10-day rest period. Sulphapyridine is the next drug of choice.

The authors conclude that although the lesions of pyoderma gangrenosum as seen in their classic form are distinctive, the aetiology of the disease remains obscure. *G. B. Mitchell-Heggs*

750. **The Treatment of Fungous Infection of the Skin with Nicetin**

A. J. BRADY and J. D. GRAY. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **76**, 725–729, May 1, 1957. 4 figs., 2 refs.

At the Halifax Infirmary, Halifax, Nova Scotia, the authors have tried " nicetin ", a product formerly known as CMA–37, with the formula αα-dichloro-N-[β-(hydroxymethyl)-*p*-nitro-phenacyl] acetamide, in the treatment of 35 cases of fungous infection of the skin, scalp, or nails. The drug was applied either in the form of a 2% ointment or as a 2% solution in propylene glycol. Cultures for fungus were made before and after treatment. All but 6 were cases of tinea corporis or tinea capitis in which *Microsporum audouini* was the commonest pathogen found on culture. Treatment was given for periods varying from 5 to 19 days and sterile cultures were obtained at the end of this time. Sterile cultures were also obtained in 2 cases of onchomycosis (although the nailbed was permanently damaged), in 2 cases of dermatophytosis, and in one of sycosis barbae. No improvement was noted in one case of hairy tongue due to infection with *Candida albicans*.

On the basis of the lytic changes observed in the local treatment of squamous epithelium in this series it is postulated that the haematuria which has been reported following oral ingestion of nicetin may have arisen from lytic changes in the transitional epithelium of the urinary bladder. It is considered that this hypothesis, if con-

firmed, will restrict the use of nicetin in the treatment of systemic fungal infections. It is advised that topical treatment should not be continued for longer than 10 days. *R. R. Willcox*

751. **Urticaria profunda dolorosa migrans.** (Urticaria profunda dolorosa migrans)
A. STÜHMER. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **135**, 272–279, March 16, 1957. 5 figs.

From the University Skin Clinic, Freiburg, is presented the case history of a 31-year-old man from whom a spindle-cell sarcoma in the neck was surgically removed, the operation being followed by intensive radiotherapy. The patient was free of symptoms until a year later, when he developed extremely painful, circinate, raised weals on the scalp, the affected areas being hard, deep-seated, and moderately well demarcated. There was no evidence of inflammation and the skin surface remained intact.

It was assumed that a recurrence of the growth was responsible, but histological examination showed no evidence of malignancy, the sections being characterized by gross interstitial oedema. The swellings changed their position slowly and eventually invaded the face and one shoulder. During this time the patient complained of severe neuralgic pains in the region of the trigeminal and intercostal nerves which were thought to be due to mechanical pressure by the lesions on these nerves. Several methods of treatment were tried, including ACTH and cortisone, and also radiotherapy, this last appearing to be the most successful; at all events the skin cleared completely after some 8 months. The aetiology of this condition is unknown. It is suggested that it might be named "urticaria profunda dolorosa migrans". Its possible connexion with the spindle-cell sarcoma remains an open question, which may be discussed in a later report. *G. W. Csonka*

752. **Benign Pemphigoid? A Report of Seven Cases with Chronic, Scarring, Herpetiform Plaques about the Head and Neck**
L. A. BRUNSTING and H. O. PERRY. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **75**, 489–501, April, 1957. 5 figs., 10 refs.

Following the observation of 7 cases at the Mayo Clinic over periods of one to 5 years, the features are described of a clinical syndrome which appears to be related to both dermatitis herpetiformis and mucosal pemphigoid. Its characteristics included the presence of recurring, grouped, vesicular plaques about the head and neck associated with local irritation and leading ultimately to scarring. The benign course of the eruption was interrupted occasionally by generalized exacerbations of a similar nature, lasting several weeks and clearing spontaneously. Only in one case were muscosal lesions seen during the period of observation. In 6 cases there was evidence of allergy of varying degree.

Histologically, there was no trace of acantholysis, but merely subepidermal bullous formation with a dense dermal infiltrate containing numerous eosinophil granulocytes. Other laboratory investigations included virus studies, patch and intradermal sensitivity tests, and examination of the urine for porphyrins, but all gave negative results.

It is considered that this syndrome is probably most readily classified with the benign pemphigoid group of skin disorders. *Allene Scott*

753. **Fluorescence Microscopy and the "Acantholytic" Cell**
A. JARRETT. *British Journal of Dermatology* [*Brit. J. Derm.*] **69**, 117–129, April, 1957. 11 figs., 14 refs.

In a brief discussion of the literature of pemphigus vulgaris and other bullous diseases the author, writing from University College Hospital Medical School, London, points out that acantholytic cells have been described in pemphigus vulgaris, pemphigus vegetans, pemphigus foliaceous, Darier's disease, and the benign familial pemphigus of Hailey and Hailey, in all of which the blister is intra-epidermal. In dermatitis herpetiformis (D.H.), including pemphigoid or benign pemphigus vulgaris, however, in which the blister is subepidermal, acantholytic cells have not so far been described. The author has therefore studied 5 cases of histologically typical D.H. and 5 of pemphigus vulgaris by means of fluorescence microscopy. The method is fully described. Various fluorochromes were used, of which primulin, acridine orange, double staining with thioflavine S and T, or rhodamine 3 G.O. and thioflavine S were found most suitable. These stains clearly demonstrated acantholytic cells in pemphigus vulgaris. In all the cases of D.H., cells with the same fluorescence as those in the pemphigus blisters could be demonstrated, as also in sections stained with haematoxylin and eosin, especially by phase contrast microscopy. By means of these stains the sequence of events occurring in acantholysis could be reconstructed; it was shown that there is a progressive loss of fluorescence concurrent with a process of cytoplasmatic keratinization. (Stages of this process, graded 1 to 4, are summarized in a table.) The same process occurs in both conditions, but more quickly in D.H.

Sections of skin from a case of Darier's disease and of normal skin in which artificial acantholysis had been produced by treatment with trypsin showed acantholysis of Stages 1 and 2 only; no acantholytic cells were seen in a case of erythema multiforme and only a few such cells in one of several cases of epidermolysis bullosa. It is therefore concluded that the presence of acantholysis cannot be used to distinguish pemphigus vulgaris from D.H. and pemphigoid. In the subepidermal blister of the latter conditions the greater intrabullous pressure probably causes more rapid degenerative changes so that Stage 4 is reached sooner; in this stage the cells stain only weakly with eosin under ordinary light and can no longer be recognized as epidermal cells. In one case of clinical pemphigus vulgaris in which the patient had tense blisters no acantholytic cells were seen by ordinary light, but such cells in Stage 4 were seen under ultraviolet light. Thus even in an intraepidermal blister acantholytic cells may not be seen if the pressure is high enough. Finally 4 cases of dermatitis herpetiformis are briefly described in which early biopsy revealed the presence of typical acantholytic cells. *F. Hillman*

Paediatrics

754. **Congenital Malformations and Maternal Rubella**
D. B. PITT. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 233–239, Feb. 23, 1957. 1 fig., 19 refs.

A series of 20 cases of pregnancy complicated by rubella were seen at the Royal Women's Hospital, Melbourne, over a recent 8-year period. In 16 cases rubella occurred during the fourth month of pregnancy or earlier, and in 14 of these adequate follow-up was possible. Of the 14 mothers 10 had normal children. One child had a doubtful abnormality (possibly pulmonary stenosis) and 3 were definitely abnormal, one having anencephaly and bilateral cataract, the second megalocornea, atrophy of the iris, and patent ductus arteriosis, while the third, who died in the neonatal period, was found at necropsy to have several cardiac defects. The ages of the children at follow-up examination was 2 to 8 years.

The author notes that in this series the incidence of abnormality following rubella in the first 4 months of pregnancy (3 out of 14 cases) is in agreement with that noted by other workers in Britain, Sweden, and the United States, but is not in accord with the high figure of earlier surveys reported from Australia. [No specialist examinations of the hearing of these children were carried out.] *C. O. Carter*

NEONATAL DISORDERS

755. **Studies of Respiratory Insufficiency in Newborn Infants. II. Correlation of Hydrogen-ion Concentration, Carbon Dioxide Tension, Carbon Dioxide Content and Oxygen Saturation of Blood with Trend of Respiratory Rates**
H. C. MILLER, F. C. BEHRLE, N. W. SMULL, and R. D. BLIM. *Pediatrics* [*Pediatrics*] **19**, 387–398, March, 1957. 6 figs., 15 refs.

In this further study, reported from the University of Kansas Medical School, Kansas City, of the relationship between the blood gas chemistry and respiration in newborn infants the respiratory rates of 61 normal full-term and premature infants were counted during the first 4 days of life for one minute every 15 minutes for the first hour, every 2 hours for the next 47 hours, and then every 4 hours for the next 48 hours. The infants were divided into three groups: (1) those that breathed at approximately 40 respirations per minute; (2) those with a high rate of respiration during the first hour which subsequently decreased significantly; and (3) those whose respiratory rate increased significantly after the first hour. "Significant" is defined as a change of 15 respirations or more per minute as compared with the mean respiratory rate during the first hour after birth. The *p*H, CO_2 content and tension, and the oxygen saturation were estimated in femoral vein blood taken during the first 6 hours of life and between the 7th hour and 7th day.

Previous studies had shown that, clinically, infants in the first and second groups make good progress and do not develop respiratory distress, whereas of those in Group 3 about one-half develop cyanosis or other serious clinical symptoms and of these about one-quarter die. The differences in the blood findings in Groups 1 and 2 were negligible and these results were therefore combined and compared with the findings for Group 3. [The detailed results are depicted in six graphs for which the original paper should be consulted.]

Satisfactory oxygenation of the blood would appear to be more easily achieved than is the maintenance of normal acid–base balance. Respiratory acidosis occurred with statistically significant greater frequency in infants with increased rate of respiration and sometimes persisted for several days. A study of the role of the tidal volume in this respiratory acidosis carried out on 4 infants in Group 3 showed it to be below the normal level in 16 out of 17 measurements; yet 3 out of these 4 infants were able to decrease the *p*H of the blood to normal levels, and to reduce the CO_2 tension and their respiratory rates to normal. Severe respiratory insufficiency is closely associated with a low tidal volume and uncomplicated respiratory acidosis, but clinical recovery does occur with restoration of the acid–base balance to normal and satisfactory oxygen saturation, even though the tidal volume remains abnormally low. How this is achieved is a matter for speculation and for further study. It is suggested that possible mechanisms may be an increase in effective alveolar ventilation and a change in the alveolar wall such as to allow diffusion of CO_2 and oxygen with greater ease. *David Morris*

756. **A Survey of Cord Blood. Haemoglobin Levels in Normal Infants**
D. G. CHALMERS, A. J. SMITH, and A. R. H. WORSSAM. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **106**, 65–67, 1957. 9 refs.

The cord blood haemoglobin level of 280 healthy infants was estimated. The levels ranged from 11·5 g. per 100 ml. to 21·0 g. per 100 ml. with a mean of 15·45 g. per 100 ml. No correlation was found between the haemoglobin level and the sex of the infant, birth weight, maturity, maternal age, parity, or a history of previous miscarriages. The results are compared with those of similar surveys performed elsewhere.—[Authors' summary.]

757. **ABO Incompatibility in the Etiology of Hemolytic Disease of the Newborn**
W. E. COPELAND, N. VORYS, and J. C. ULLERY. *American Journal of Obstetrics and Gynecology* [*Amer. J. Obstet. Gynec.*] **73**, 1045–1053, May, 1957. 1 fig., 23 refs.

758. **Physiologic Studies on the Cardiovascular Status of Normal Newborn Infants (with Special Reference to the Ductus Arteriosus)**

F. H. ADAMS and J. LIND. *Pediatrics* [*Pediatrics*] **19**, 431–437, March, 1957. 1 fig., 15 refs.

From the Wenner-Gren Cardiovascular Research Laboratory, Stockholm, comes this interesting report of the investigation of the cardiovascular physiology of young infants, in which 8 normal newborn infants, 5 males and 3 females, were examined between 7 hours and 14 days of birth by cardiac catheterization under basal anaesthesia, standard and unipolar electrocardiography, and by *x*-ray examination for heart volume. Blood samples were taken for determination of oxygen content and records were made of the pressure in each of the major vessels and chambers entered, for which a 2-channel jet recording "mingograph" was used.

The changes in the heart volume with age appeared to fall within the normal range. The electrocardiogram was also within the range of the expected normal, with one minor exception. Hypertension in the right ventricle and pulmonary artery was found in the majority of the infants studied and was present for 3 to 4 days after birth, gradually falling to the normal value during the next few days; previously it had been supposed that this took place within several minutes of birth. The highest reading obtained was 50/0 mm. Hg in the right ventricle and 50/10 mm. Hg in the pulmonary artery. Analysis of the oxygen content of the blood showed a significant left-to-right shunt of blood in the pulmonary artery in 5 of the 7 infants in whom the pulmonary artery was entered, indicating that the ductus arteriosus remains functionally patent with predominantly a large left-to-right shunt for several days. *David Morris*

759. **Ichthyosis Congenita**

A. B. FALK, H. S. TRAISMAN, and G. J. AHERN. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] 93, 259–262, March, 1957. 3 figs, 7 refs.

The term ichthyosis congenita is here used by the authors to include all the three types of the disorder as described by Riecke in 1900, namely, the harlequin foetus, which always dies, the infant enclosed at birth in a collodion-like sheath, who may die, and the infant with minimal findings at birth, who usually lives. From the Children's Hospital, Chicago, 6 cases of varying degree are described; 4 of these patients died and 3 of them were examined post mortem. Each showed a similar skin condition, that is, one of lamellar exfoliation. The outer sheath of the undenuded skin consisted of a thick stratum corneum with marked parakeratosis. The sheath split away through the deepest keratotic layer and keratotic plugs were found in the gland orifices; the remaining epidermis was thin and partially cornified, but the dermis was normal. There was very little epidermis in the denuded areas; the sweat glands were plugged, and the deeper layers showed some lymphocytic infiltration. One of the patients had congenital heart disease together with other abnormalities.

Of the 2 surviving children one had a parchment-like skin at birth, but extensive scaling started shortly afterwards and persisted up to the age of 2 years; this child now has generalized ichthyosis with varying erythema. The other surviving child also had a parchment-like skin which split at the age of 3 days. After 3 weeks the child was normal, except for a dry skin, but later, however, generalized ichthyosis developed. Both children were otherwise normally developed. Each of these 2 surviving children was a sibling of one of the patients who died. The condition is an inherited trait of the recessive type. *E. H. Johnson*

760. **Pemphigus Neonatorum Caused by *Staphylococcus aureus* Type 71**

W. A. GILLESPIE, R. C. POPE, and K. SIMPSON. *British Medical Journal* [*Brit. med. J.*] **1**, 1044–1046, May 4, 1957. 18 refs.

A small epidemic of pemphigus neonatorum at a maternity hospital in Bristol was found to be due to *Staphylococcus aureus* phage Type 71. An investigation of staphylococcal cross-infection was fortunately in progress in the nursery wards at the time the outbreak started. Two months previously a new nurse in the department was found to be a persistently heavy nasal carrier of Type 71 penicillin-resistant staphylococci. It later transpired that she had had impetigo 3 years previously. The first baby to develop pemphigus had been in her special care for some days. Subsequent cases were believed to be caused by cross-infection from the first case, the organisms probably being transferred by contact by members of the staff and through the agency of blankets. The authors recommend that methods to limit the spread of infection should include the disinfection of bedclothes after use, the use of a disinfectant hand cream, and the application of a suitable antibiotic cream to the nostrils of suspected nasal carriers. *E. G. Rees*

761. **Hirschsprung's Disease in the Neonatal Period. A Report of Five Cases, Four of Which Involved the Small Intestine**

D. H. BOWDEN, A. M. GOODFELLOW, and J. D. MUNN. *Journal of Pediatrics* [*J. Pediat.*] **50**, 321–326, March, 1957. 4 figs., 5 refs.

The few cases reported in the literature of Hirschsprung's disease affecting the small intestine as well as the colon prompted the authors, in this paper from the Hospital for Sick Children, Toronto, to describe 5 cases of the disease in infants, in 4 of which there was ganglion aplasia of the whole large bowel and a portion of small bowel. In the fifth case peritonitis developed without actual perforation of the bowel, post-mortem examination revealing the more usual features of Hirschsprung's disease—that is, myenteric plexus defect in the colon distal to the splenic flexure. Of the 5 infants, 4 died in the first month of life and one at 3½ months.

The authors stress the importance of this condition as a cause of intestinal obstruction in early infancy, and discuss the difficulties of diagnosis. They consider that lack of awareness of the condition and the fact that most infants with involvement of a long segment of intestine die in the neonatal period mitigate against early diag-

nosis. In their view the condition is not always hopeless, and ileostomy is the only reasonably immediate procedure. *Margaret D. Baber*

762. **Haematogenous Osteitis in the Newborn**
J. Boyes, A. E. Bremner, and G. A. Neligan. *Lancet* [*Lancet*] **1**, 544–548, March 16, 1957. 7 refs.

Stating that haematogenous osteitis "is still an important cause of crippling deformity, and a potential cause of death, in the newborn", the authors discuss a series of 40 cases of the disease seen over a period of 8 years at the Royal Victoria Infirmary, Newcastle upon Tyne (University of Durham). In 21 cases the condition was judged to be severe and in 19 mild, although the authors point out that a precise clinical definition of severity appears to be unattainable. Pathogenic organisms, most often *Staphylococcus aureus*, were cultured from the pus in all but 8 cases. Of the 24 strains of *Staph. aureus* 16 were resistant to penicillin *in vitro*, but all strains of *Streptococcus haemolyticus* (5 cases) and of pneumococci (2 cases) were sensitive to this antibiotic, while the *Escherichia coli* isolated in one case was sensitive to streptomycin. The course of the disease varied, ranging from mild with a tendency to spontaneous recovery to severe with pyaemia, and did not depend upon the severity of the condition when first seen. The osteitis caused destruction of the hip-joint in 4 cases in which there was delay varying from 5 to 27 days between signs in the upper femur and the start of treatment. In the 21 severe cases the average delay before treatment was 8 days.

Among the first signs were: swelling, sometimes with discoloration of skin, in 14 cases; irritability, worse on handling, in 13 cases; "pseudoparalysis" in 9 cases, while in 4 of the severe cases there were signs of general infection. Except for these last, the type of sign could not be related to mildness or severity of the course. Bone tenderness was apparent on admission to hospital. The delay was often due to failure to realize the importance of the signs noted. The authors emphasize that tenderness, immobility, or swelling of a limb (if not due to trauma) in the newborn is likely to indicate infection. The primary site of such infection is more likely to be in bone than in subcutaneous tissue, with possibly serious complications in a young baby.

In the treatment marked swelling of soft tissues was taken as indication for aspiration of pus from the bone through a short, wide-bore needle. Penicillin, 50,000 units, or streptomycin, 50 mg., was then injected into the joint if this was involved. Sequestra were removed in 2 cases. Most of the patients were not immobilized. In general penicillin was the antibiotic used initially, in doses of 25,000 to 50,000 units 3-hourly by intramuscular injection, this being reduced to 6-hourly if progress was good. Chlortetracycline was also given until the results of sensitivity tests were known. The duration of treatment in 18 of the severe cases ranged from 21 to 116 days (mean 41 days). In 25 of 31 cases treated for 19 to 116 days (mean 34 days) healing was complete clinically and radiologically; in the remaining 6 cases there was recurrence of the infection. In 7 cases treated soon after onset for only 4 to 13 (mean 7) days the infection recurred but later responded to further treatment. One patient died, and of the survivors 10 were left with abnormal joints.

The authors recommend antibiotic treatment for a minimum of 3 weeks. Of the 23 strains of *Staph. aureus* isolated only 2 were insensitive to streptomycin, leading the authors to suggest that this antibiotic might therefore have been preferable to chlortetracycline as a paired antibiotic with penicillin. The cases in which treatment failed are discussed in detail.

[This paper again underlines the dangers of staphylococcal infection in the newborn and the problems encountered in the use of antibiotics for its treatment.] *Pamela Aylett*

CLINICAL PAEDIATRICS

763. **The Relation Between Birth Weight and Weight Gain Throughout the First Year**
J. Millis and Tye Cho-Yook. *Annals of Human Genetics* [*Ann. hum. Genet.*] **21**, 289–292, March, 1957. 6 refs.

Correlation analysis is introduced to study the relationship between birth weight and "weight gain" through each 4-week interval in the first year of life. The coefficients so derived are found to fluctuate "non-significantly" around zero, and show no consistent pattern or trend through the first year of life for male and female alike. It is shown that, because of the independence of weight gain and birth weight, the coefficient of correlation for each sex between birth weight and weight at one year can be estimated directly from the variances of the series of weight measurements.

The following results were obtained in conformity with those of other authors on the subject: (*a*) males gain significantly more weight than females in the first year of life, (*b*) weight gain in the first year of life is not found to be dependent on birth weight among infants of the same sex, (*c*) there is a fair degree of correlation between birth weight and weight at one year.—[Authors' summary.]

764. **Comparative Frequency of Detection of Enteropathogenic *E. coli*, *Salmonella* and *Shigella* in Rectal Swab Cultures from Infants and Young Children**
M. L. Cooper, H. M. Keller, and E. W. Walters. *Pediatrics* [*Pediatrics*] **19**, 411–423, March, 1957. 11 refs.

In an attempt to determine the comparative frequency of infections due respectively to *Salmonella*, *Shigella* and *Escherichia coli* in children routine rectal swabs were taken of all children (2,865) admitted to the Children's Hospital of the University of Cincinnati over a 2-year period and cultured for these organisms, including the 9 serotypes of *E. coli* described by Ewing and Edwards. Positive cultures were obtained in 361 patients, 85 of *Salmonella*, 88 of *Shigella*, and 188 of one of the 9 serotypes of *E. coli*. Cultures were negative in 889 patients in whom diarrhoea was present, and also in 1,615 patients without diarrhoea. In all, 17 different serotypes of

Salmonella were cultured, *S. Oranienburg* occurring in 24 and *S. typhimurium* in 19; diarrhoea occurred in all but 4 of the 85 patients with this infection. In the *Shigella* group, 53 cultures showed *Sh. soneii* and the rest were distributed amongst the 5 types of *Sh. flexner*; diarrhoea was present in 82 of the 84 patients in this group for whom adequate information was available. Of the 188 infants with *E. coli* infection strain O55 B5 occurred in 63 cases, O111 B4 in 26, O126 B16 in 25, and O26 B6 in 22 patients; in this group diarrhoea occurred in 171 of the 186 patients for whom adequate information was available.

Of the patients with *E. coli* infection 76·9% were in the first year of life, 39·8% being under 3 months of age. The peak of infection in the *Shigella* group was in the second year at 26·1%; the incidence in the *Salmonella* group fell between these two, with a peak of 38·6% in the first year and 22·9% in the second. October and November were the months of greatest incidence for *E. coli* infections, September and October for *Shigella*, and April and July for *Salmonella* infections in the first year of the study but in September, January, and February in the 2nd year. In 15 cases more than one of the three pathogens was isolated. Swabs taken on the 3rd or 4th day after discontinuing treatment or during the 1st or 2nd week after discharge from hospital gave positive cultures in 24 of the 175 patients so examined; of these, 15 out of 41 (36·6%) occurred in the *Salmonella* group, 1 out of 38 (2·6%) in the *Shigella* group, and 8 out of 96 (8·3%) in the *E. coli* group. Only one patient infected with *Salmonella* died, none infected with *Shigella* did so, and 3 died in the *E. coli* group (type O55 B5 was present in all 3 cases); of the 595 patients with diarrhoea from whom no pathogens were isolated 9 died.

David Morris

765. **Non-tuberculous Juvenile Bronchiectasis: a Virus Disease?**

P. S. MacFarlane and R. G. Sommerville. *Lancet* [*Lancet*] **1**, 770–771, April 13, 1957. 1 fig., 9 refs.

In the morphological examination of operation specimens from children with bronchiectasis undergoing lobectomy at the Western Infirmary and Royal Hospital for Sick Children, Glasgow, the authors noted that in about three-quarters of the cases lymphoid hyperplasia was the dominant feature. This picture resembled closely the lesions of " cuffing pneumonia ", a common respiratory disease of cattle which is probably due to a virus infection. Complement-fixation tests were therefore carried out in 18 cases of bronchiectasis, before and after operation, with antigens from influenza viruses A, B, and C, the adenovirus group, and newborn pneumonitis virus (type Sendai). Serological evidence of adenovirus infection was obtained in 11 cases, in 8 of which the titre was 1:16 or over, and in one case an agent with the characteristics of an adenovirus was isolated from the resected lung tissue and hilar lymph nodes.

It is suggested that in juvenile bronchiectasis, as in influenza, the primary pathogen is a virus and that the pyogenic bacteria commonly associated with the disease are secondary invaders.

Franz Heimann

766. **The Treatment of Infantile Eczema with ACTH and Cortisone.** (Die Behandlung des Säuglingsekzems mit ACTH und Cortison)

H. Klingenfuss. *Annales paediatrici* [*Ann. paediat. (Basel)*] **188**, 226–246, April, 1957. 23 refs.

Between 1953 and 1955, 30 children with skin lesions were treated at the University Paediatric Clinic, Basle, with oral cortisone or hydrocortisone ointment, or both. [In spite of the title of the paper, none appear to have received ACTH.] Of these patients, who ranged in age from 3 months to 3 years, 23 suffered from infantile eczema, 3 from seborrhoeic dermatitis, and 4 from neurodermatitis. [In addition, 2 infants with Kaposi's varicelliform eruption were given cortisone without benefit, thus confirming the general experience that the hormone is of no value in skin disorders due to specific factors.] A good response to cortisone, shown by relief from itching within 24 to 48 hours and by regression of erythema and oedema in acutely inflamed skin patches, was obtained in the patients with infantile eczema. Those with seborrhoeic dermatitis reacted more favourably than previous reports in the literature had suggested, but they were too few in number to justify a firm conclusion. The least dramatic response to oral cortisone was seen in the neurodermatitis group, probably because, as is known, cortisone affords less relief in chronic atrophied and lichenified skin lesions, than in those which are actively inflammatory. No untoward side-effects were encountered.

The author considers cortisone therapy to be virtually harmless (except in the presence of active tuberculosis, when it is contraindicated) provided it is not continued longer than is absolutely necessary, and never for more than 3 to 4 weeks. As it tends to lower resistance to infection, its combination with an antibiotic is of advantage. Hydrocortisone ointment, too, may be combined with an antibiotic, and because only about one-tenth is absorbed through the skin, a treatment period of several weeks is permissible. Eczema recurs with such regularity when therapy is discontinued, that the percentage of permanent cures remains small. The author stresses that the classic treatment with diet, baths, lotions, and ointments must never be abandoned out of hand in favour of oral cortisone or hydrocortisone ointment, although it is of course reasonable to treat cases resistant to ordinary measures, or mild cases of generalized eczema, with hydrocortisone ointment (1½ to 2%), and severe cases, especially when they are associated with marked toxaemia, with oral cortisone. The optimum dose must be determined for each individual case. In general, one-half of the adult dose, or about 50 to 70 mg. daily, is appropriate for an infant up to one year, and three-quarters of the adult dose for infants aged one to 4 years. Later, the dose should be reduced gradually, since therapy must not be discontinued suddenly. Eradication of the suspected cause of the eczema must not be forgotten, nor the management of secondary infection neglected.

E. S. Wyder

767. **The Innocent (Functional) Cardiac Murmur in Children**

D. H. Fogel. *Pediatrics* [*Pediatrics*] **19**, 793–800, May, 1957. 17 refs.

Public Health and Industrial Medicine

768. **Methemoglobinemia from Eating Meat with High Nitrite Content**

J. D. ORGERON, J. D. MARTIN, C. T. CARAWAY, R. M. MARTINE, and G. H. HAUSER. *Public Health Reports* [*Publ. Hlth Rep.* (*Wash.*)] **72**, 189–193, March, 1957. 19 refs.

In October, 1955, 10 cases of methaemoglobinaemia occurred near New Orleans, Louisiana, the patients being children aged 1½ to 10 years (only 2 were over 5). It was found that the outbreak was due to nitrite poisoning following consumption of sausage meat products, and laboratory examination of the vomit and of remains of sausages showed that the latter contained 5,420 p.p.m. of nitrite. All patients recovered after intravenous injection of methylene blue.

Nitrites and nitrates have some preservative properties, but they are used for curing meat mainly because of their colour-fixing qualities. Bacterial action and hydrolysis break down these agents into nitric oxide, which combines with the myoglobin of the meat to form a more permanent pink colouring than the natural pigment. The ingestion of certain chemicals, including nitrites, can oxidize the haemoglobin to methaemoglobin and reduce the oxygen-containing and oxygen-carrying power of the blood. U.S. Federal regulations and many State regulations lay down a limit of 200 p.p.m. of nitrite in meat products for human consumption. The sausages incriminated in this outbreak came from the same manufacturer, and of 131 samples of assorted meat products from this source, 17 contained a concentration of nitrite in excess of the regulation 200 p.p.m., there being 6,570 p.p.m. in some instances. Investigations at the plant failed to trace the particular batch involved or to determine how the over-dosage of additive occurred, but there was some reason to suspect that a powder consisting wholly of sodium nitrate may have been added instead of the usual preparation, which is made up of only 10% nitrite and nitrate, the rest being sodium chloride.

The authors refer to 2 further cases which have since been reported in children in Florida. *J. Cauchi*

769. **Pertussis Antibody Response after Triple Antigen**

G. V. FELDMAN. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **32**, 111–113, April, 1957. 9 refs.

Infants attending a routine follow-up clinic of the University Department of Child Health, Manchester, were immunized against diphtheria, pertussis, and tetanus in approximately equal numbers with (A) a saline-suspended vaccine, and (B) a vaccine of comparable antigenic strength containing aluminium phosphate. Three monthly injections [dosage not stated] of each were given, starting when the infants were about 3 months old, blood being taken for antibody estimations one month after the last injection.

The results were much better with Vaccine B, particularly for pertussis, no less than 50% of the children immunized with Vaccine A having a pertussis agglutination titre of less than 1:16, whereas only one of these given Vaccine B had such a low titre. Results obtained in a previous series with a vaccine (C) containing double the amount of alum in Vaccine B and in which the third injection was not given until 5 months after the second, however, were considerably better than those obtained in the present series.

The author concludes that the reasons commonly advanced for using saline suspensions for the immunization of infants against these three diseases—such as the reduction of side-effects and of the risk of poliomyelitis—are inadequate and do not warrant their being used in preference to alum-containing vaccines.

W. K. Dunscombe

770. **Epidemiological Aspects of an Outbreak of Encephalomyelitis at the Royal Free Hospital, London, in the Summer of 1955**

N. CROWLEY, M. NELSON, and S. STOVIN. *Journal of Hygiene* [*J. Hyg.* (*Lond.*)] **55**, 102–122, March, 1957. 5 figs., 18 refs.

The authors give a detailed report on an outbreak of encephalomyelitis affecting more than 300 out of about 3,500 persons on the staff of the Royal Free Hospital, London, and of the various hospitals and institutions associated with it. The epidemic had an explosive character which suggested that the infective agent might be spread by a common vehicle. However, no evidence was found that either water or milk supplies were the source of infection. Bacteriological, serological, and virological investigations relating to a variety of bacteria, protozoa and viruses all gave negative results. Persons of both sexes and of all ages were attacked, but those under 30 proved more susceptible. The average incubation period was between 5 and 7 days. The case incidence was highest among nurses, and residents were at least three times more liable to be infected than non-residents. Relatives and friends as well as the husbands and wives of members of the staff were also affected. More than half the cases occurred in July and August, the beginning of the epidemic coinciding with the year's longest spell of hot, dry weather.

The clinical picture was characterized by sore throat, headache, stiffness of the neck, dizziness, blurred vision, bodily prostration, and low-grade fever. In a high proportion of cases there was enlargement of the lymph nodes, particularly in the posterior cervical triangle, with varying degrees of lympho-reticular disturbance and morphological changes in the mature lymphocytes. The Paul–Bunnell test was performed in 121 cases, in 94 of which it gave a titre of 1:40 or higher. In some cases neurological symptoms were prominent in the form of vertigo, diplopia, paraesthesiae, paresis, asthenia, and myalgia, which were often associated with apathy and depression. The cerebrospinal fluid was examined in 8

cases and showed no abnormality. Altogether, symptoms occurred in some 500 persons, of whom about 400 reported sick and 326 developed the frank syndrome. While most of the patients were ill for not more than a few days, a few had to remain in hospital for several months. Although there was some resemblance to poliomyelitis, the clinical picture was one of benign myalgic encephalomyelitis. *Franz Heimann*

771. ***Escherichia coli* (O-Types 111, 55 and 26) and Their Association with Infantile Diarrhoea. A Five-year Study**
E. I. HUTCHINSON. *Journal of Hygiene* [*J. Hyg.* [*Lond.*)] 55, 27–44, March, 1957. 7 refs.

A survey of the various strains of *Escherichia coli* associated with infantile gastro-enteritis in the Southampton area was carried out over a period of 5 years from 1949 to 1954. So far as possible the survey included all cases of gastro-enteritis in infants who had been admitted to the local hospitals or had been reported from residential nurseries and clinics under the control of the local authority, together with cases attended by general practitioners from which material was sent for examination to the Public Health Laboratory. Up to May, 1953, only two types of *E. coli*, O 55 and O 111, were found to be associated with infantile gastro-enteritis, but later a third strain, O 26, was added. Faecal specimens from 1 234 individuals were examined for these three types: type O 55 was isolated from 159 infants, of whom 126 had acute symptoms, type O 111 from 66 infants, of whom 56 had enteritis, and type O 26 from 14 infants, of whom 12 had enteritis. The average isolation rate of type O 55 during epidemic periods amounted to 37·2% and during non-epidemic periods to 1·2% for type O 111 the corresponding figures were 26·9% and 1·4% respectively.

The clinical picture did not differ as between the three bacterial types of infection, varying in each case from the very grave case of gastro-enteritis to the simple excreter without clinical evidence of disease. Symptomless excreters were found in all age groups, being more frequent among children above one year of age but also occurring among infants as young as 2 weeks. At the time of an epidemic the proportion of symptomless excreters to cases of clinical disease in all age groups was much higher than during non-epidemic periods.

The determination of the H antigen carried by organisms of type O 55 during an epidemic in the spring of 1952 revealed the presence of two subtypes, H2 in 51 cases and H7 in 3 cases. During a similar outbreak in 1953 due to infection with type O 111 two subtypes, H2 and H12, were found, but during a further type-O 111 outbreak in 1954 only H12 was identified. The various strains of *E. coli* isolated were able to survive for long periods outside the body; in ward dust naturally contaminated the organisms remained viable for up to 12 days, survival being longer under shaded conditions than in direct sunlight.

The pattern of the outbreaks described suggested a gradual enhancement of virulence of the two main types of *E. coli* concerned, with local spread followed by wide dispersal through the district, and then by reversion to the poorly invasive type. *Franz Heimann*

772. **Environmental Studies of Endemic Enteric Virus Infections. I. Community Seroimmune Patterns and Polio-virus Infection Rates**
J. L. MELNICK, M. WALTON, P. ISACSON, and W. CARDWELL. *American Journal of Hygiene* [*Amer. J. Hyg.*] 65, 1–28, Jan., 1957. 6 figs., 21 refs.

The authors report from Yale University that in collaboration with the Communicable Disease Center of the U.S. Public Health Service, from 1951 until 1953 the incidence of poliovirus infections, as indicated by isolation of the viruses or the development of antibodies against them, was studied in sections of the normal population in two towns each of about 100,000 inhabitants, namely, Charleston, West Virginia, and Phoenix, Arizona. Neither place had recently experienced large-scale outbreaks of the disease, its incidence in Charleston having been seasonal, and in Phoenix of more even occurrence. In each town two well-separated districts of contrasting socio-economic status were selected and the hygienic conditions of each household with children under 15 years old were assessed. Blood was collected from as many persons as possible in each household each spring and autumn, and faeces were collected monthly from all children in these households who were under 5 years of age. In Charleston 239 poorer and 521 better-off households containing respectively 1,143 and 1,929 persons were investigated, in Phoenix the corresponding numbers were 384 and 301, involving 1,755 and 1,046 persons respectively.

Monkey kidney tissue-cultures were employed for virus isolation and neutralizing antibody titres were estimated by a colorimetric method using disposable styrene panels. Antibodies were found to develop at an earlier age in persons living in the poorer districts in both cities: thus 50% of the children aged 5 to 9 years in these districts had antibodies against one or more types of the virus, whereas in the better-class districts this rate was not reached until early adulthood. The contrast between households with good and bad hygiene in a particular district was less marked. Antibody titres were lower in the higher age groups, although the adults from the better districts showed higher titres, their infection having been acquired more recently. Poliovirus was isolated from 2·8% of the faecal specimens from the poorer districts and from 0·6% of specimens from the better districts. No clinical poliomyelitis occurred in any of the households studied; yet it was apparent from the evidence of virus isolation and the development of antibodies in persons previously lacking them, that inapparent infections had occurred at irregular intervals throughout the 3 years of the study, sometimes involving 50% of the susceptible population. These silent infections also took place at an earlier age among the inhabitants of the poorer districts than among those living in districts of good hygienic standards. When the amount of clinical poliomyelitis due to a particular type of virus occurring in municipal areas adjacent to those studied was compared with the amount of subclinical infections, the ratios of infection to cases varied widely in different years. Roughly estimated ratios of inapparent infections per clinical case ranged from 32 to 145 in Phoenix and from

70 to 496 in Charleston. In both towns Type 1 virus was most frequently associated with clinical disease, but in the poorer districts of Phoenix Type 3 was predominant in 1952. *J. E. M. Whitehead*

773. **Environmental Studies of Endemic Enteric Virus Infections. II. Poliovirus Infections in Household Units**
P. ISACSON, J. L. MELNICK, and M. WALTON. *American Journal of Hygiene* [*Amer. J. Hyg.*] **65**, 29–42, Jan., 1957. 2 figs., 24 refs.

In the second part of this study a closer investigation was made of the spread of poliovirus within households. For this, the results for both types of district in Phoenix and in Charleston were combined. In sera collected from 21 normal children under 5 years of age from whom poliovirus was isolated 8 to 15 weeks later, no neutralizing antibody titres of 1 in 10 or greater were found against the infecting type of virus. For comparison, the prevalence of titres of 1 in 10 or greater of poliovirus neutralizing antibody in the children whose stools yielded Coxsackie or ECHO viruses, and in the whole group from which faecal specimens were collected, ranged from 25 to 37% according to the virus type. Of 17 children from whom a specimen of serum was obtained after isolation of the virus, 16 showed a rise in antibody titre against the type of virus responsible for the subclinical infection, and a number showed rises against heterologous types. In the single instance where no rise was found, there was suggestive evidence that contamination of the faecal specimen had occurred.

The spread of subclinical infection in a household was assessed by assuming arbitrarily that the initial infection had occurred in the youngest member who showed laboratory evidence of infection. Evidence of spread was provided by virus isolation or by significant changes in antibody titre, and was found in 60 to 70% of " susceptible " contacts, that is, those with neutralizing antibody titres of less than 1 in 10 against the infecting type of virus before its introduction into the household. The presence of antibodies against heterotypic polioviruses before introduction of the infection could not be shown to influence the secondary attack rate, nor was it appreciably affected by the ages of the contacts or the socio-economic conditions of the district in which they lived—although it is admitted that the numbers involved were not large. *J. E. M. Whitehead*

774. **Observations on Natural Poliovirus Infections in Immunized Children**
H. M. GELFAND, J. P. FOX, and D. R. LEBLANC. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **47**, 421–431, April, 1957, (Part 1). 22 refs.

Protection against disease and protection against infection are not necessarily synonymous; hence specific immunity following vaccination against poliomyelitis may obviate the serious consequences of infection, without influencing the spread of the virus within the population unless it also influences the incidence or course of alimentary infection. Passive immunity to poliomyelitis, whether the result of gamma globulin injection or persistence of maternal protection, appears to have no effect on alimentary infection. On the other hand, immunity resulting from previous infection markedly inhibits subsequent alimentary infection.

A preliminary report on the incidence of alimentary infection following vaccination is presented, the authors having studied a group of 118 families from three areas in Louisiana, which were representative as regards race economic status, and size of family. Stools were collected twice a month from children under 15 years, and blood specimens were taken before and after each inoculation and twice a year thereafter. Inoculation was by two injections at intervals of one month, followed by a booster dose 10 months after the second. Study of the serological response to the vaccine is not yet complete, but, the authors point out, it was obvious that the responses to the three types of vaccine were not equal.

In the 7 months (February to August, 1956) following vaccination there were 38 episodes of primary infection among the families under observation. This figure was not statistically different from that recorded for 12 months in 1955, and suggests that vaccination does not affect the frequency of household infection. In these 38 episodes 129 children under 15 years were exposed to risk. Preliminary results only of stool examination were available, but it was found that of the 86 children and 7 adults who had no natural immunity before vaccination, only 9 children and 4 adults escaped infection. It was also found that 11 of the 43 naturally immune children and 5 of the 72 naturally immune adults were re-infected. These infections were demonstrated either by the serological response or the results of stool examination. All except 3 of the children known to be experiencing a primary infection were excreting the virus, as also were 9 with a re-infection. Only 2 of the latter group showed virus in the stool on more than one occasion, whereas many of the children with primary infection excreted the virus on two or more occasions. The duration of virus excretion did not appear to be materially affected by vaccination nor did it appear likely that the amount excreted was affected. The corrected mean duration of virus excretion following primary infection was 37·7 days after vaccination compared with 51 days without vaccination. *E. H. Johnson*

INDUSTRIAL MEDICINE

775. **An Outbreak of Weaver's Cough Associated with Tamarind Seed Powder**
R. MURRAY, I. DINGWALL-FORDYCE, and R. E. LANE. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **14**, 105–110, April, 1957. 8 refs.

This paper reports an outbreak of cough and dyspnoea among weavers of spun rayon and among cotton velvet cutters. Before weaving the warp yarn is normally treated with a sizing agent to strengthen it. A new factor common to both processes was the use of a size made from powdered tamarind seed kernel. In January, 1956, 3 months after the new size had been introduced, the sickness rate in one weaving shed was found to have risen very markedly. In this mill it was possible to compare two groups of workers, one which had been directly

exposed to the tamarind size and the other which had not. The entire population of the one weaving shed involved, 180 men and 208 women, were interviewed. Analysis showed that the women who had been exposed had a highly significant excess of absenteeism ($P<0.001$) and that this excess could be attributed to complaints of cough with or without breathlessness. [The small number of men exposed did not allow of useful comparison.] There was no evidence that those who had a history of previous chest illness (for example, chronic bronchitis) were specially affected and the trouble was seen equally in workers of all age groups.

The symptoms ranged from a dry throaty cough to acute and severe respiratory distress. An irritable cough, with dyspnoea, tightness of the chest, and production of a thick purulent sputum were common and many of those affected also complained of feverishness, headache, and sore eyes. There were two characteristic features: (1) a minimum period of exposure of at least 2 weeks appeared to be necessary before symptoms supervened; and (2) in many cases when the patient returned to work after sickness absence the symptoms recurred as badly as ever within a few hours.

The condition appeared to be a reaction to a constituent of the new size. Preservatives were used in the powder but for various reasons they were not considered likely to have been responsible for the phenomenon. This is attributed to the tamarind seed powder itself and is thought to have an allergic basis. The authors recommend further work to confirm these hypotheses.

R. E. Lane

776. **Health Hazards Encountered in Repair of Jet Aircraft Fuel Cells**

A. R. LOMBARDI and A. S. LURIE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **164**, 531–533, June 1, 1957. 1 fig., 5 refs.

777. **Chlorine Dioxide. Toxicity in Animal Experiments and Industrial Risks**

T. DALHAMN. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **15**, 101–107, Feb., 1957. 4 figs., 4 refs.

Chlorine dioxide is being increasingly used in industry as a bleach, for instance, for paper pulp. The maximum allowable concentration has been estimated as 1 part of ClO_2 per million parts of air (1 p.p.m.), but in this paper from the Swedish National Institute of Public Health evidence is offered that the figure should be not more than 0·1 p.p.m. The physical properties of the gas and the liquid (boiling point 11° C.) are described, with emphasis upon the explosive hazard, and details are given of Giertz's method for the determination of the concentration of ClO_2 in air. Rats exposed for 4 hours daily to a concentration of 10 p.p.m. developed copious secretion from the eyes and nose and respiratory distress; all died within 14 days. Necropsy showed severe purulent bronchitis, pulmonary oedema, and patches of bronchopneumonia, while the liver and kidneys were congested. Rats exposed for 5 hours daily to a concentration of 0·1 p.p.m. were unaffected.

Industrial investigations were carried out in a paper pulp works and a flax spinning mill. The atmospheric concentration of ClO_2 was generally less than 0·1 p.p.m. and the workers exposed showed no ill effects. The highest reading was 0·6 p.p.m., which was derived from a small test tank in the flax mill. Men working here had apparently been exposed on two occasions to a toxic concentration of the gas and had shown symptoms of exposure to a respiratory irritant—cough, with bubbling sounds in the chest and some difficulty in breathing, rhinorrhoea, and, in one case, epistaxis, while 2 men had suffered headache and vomiting. These symptoms had subsided within a week. *M. A. Dobbin Crawford*

778. **Heinz-body Formation after Exposure to Aniline and to 2:4-Dichlorophenol. Role of Catalase and Peroxide**

L. MAGOS. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **15**, 148–151, Feb., 1957. 1 fig., 22 refs.

An inquiry was carried out at the State Institute of Occupational Medicine, Budapest, into the formation of Heinz bodies *in vivo* as a result of poisoning by chemicals which inhibit catalase. Heinz bodies are formed *in vitro* by the addition of hydrogen peroxide to erythrocytes, yet cyanide, an intense catalase-inhibiting poison, does not cause the production of Heinz bodies *in vivo*, probably because it inhibits the peroxide-generating system. Similarly, 2:4-dichlorophenol is an intense catalase-inhibitor, but does not produce Heinz bodies *in vivo*. *In vitro*, however, Heinz bodies in quantity have been produced by the action of 2:4-dichlorophenol, so that it presumably does not inhibit peroxide formation and another reason must be found for its failure to produce Heinz bodies *in vivo*.

The catalase-inhibitory effect of 2:4-dichlorophenol was therefore compared with that of aniline which, though but a mild catalase-inhibitor, causes *in vivo* the formation of both methaemoglobin and Heinz bodies. By the method of Goldacre and Galston, which is described in detail, using as catalase a haemolysate of erythrocytes, the author found that aniline at 1 to 2×10^{-2} M concentration and 2:4-dichlorophenol at 8 to 9×10^{-9} M concentration each inhibited catalase activity *in vitro* to an extent of about 50%. By the addition of peroxide and catalase continuously to the aniline solution oxidation products were formed which had a more intense catalase-inhibiting effect than the original aniline solution. Catalase, therefore, has an important function in increasing the toxicity of aniline. On the other hand when catalase and peroxide were added continuously to the 2:4-dichlorophenol solution the oxidation products formed were comparatively inactive, and the catalase-inhibiting action of the solution was much diminished.

M. A. Dobbin Crawford

779. **Health Hazards in Industry from Exposure to Trichlorethylene.** (Gesundheitliche Gefahren in der Industrie bei Exposition für Trichloräthylen)

A. ANDERSSON. *Acta medica Scandinavica* [*Acta med. scand.*] Suppl. 323, 1–220, 1957. 16 figs., bibliography.

Anaesthetics

780. **Anaesthesia for Mitral Valvotomy. The Evolution of a Technique**

T. C. GRAY and J. E. RIDING. *Anaesthesia* [*Anaesthesia*] **12**, 129–147, April, 1957. 1 fig., 36 refs.

The authors review the anaesthetic techniques adopted at the Liverpool Chest Surgical Centre for mitral valvotomy between October, 1950, and November, 1955, in 371 cases (out of over 420) for which detailed records were available. The paper shows the gradual evolution of the present technique, the 9 anaesthetists concerned each independently following the same line of development, though not necessarily at the same rate. The cases are divided into 7 groups in chronological order as follows, the difference between them being mainly in terms of premedication and method of induction.

Group	No. of Cases	Premedication	Induction
1	10	Morphine and atropine	Thiopentone
2	42		Pethidine (i.v.)→thiopentone ($\frac{1}{4}$)
3	42		Pethidine (i.v.)→thiopentone (all)
4	34		Pethidine (i.v.)→N_2O–O_2→thiopentone
5	37	Promethazine, pethidine, atropine, and/or, scopolamine	Unassisted N_2O–O_2 (14 cases)
6	96		Unassisted N_2O–O_2 (73 cases)
7	110	Papaveretum and hyoscine	Unassisted N_2O–O_2 (90 cases)

Of the 371 patients, 24 (6·5%) died before leaving hospital. The cases in which there was a possibility, however remote, that anaesthesia might have contributed to the death (for example, where death occurred from heart failure within 48 hours of operation if there had been difficulty in maintaining oxygenation or blood pressure during anaesthesia, or even later if anaesthesia might have contributed to the downhill course) amounted to 10 (2·7%).

The authors show that there is some reason to suppose that the use of supplementary intravenous drugs, such as thiopentone or pethidine, may contribute to the mortality of this operation, and they have therefore evolved the following technique of gaseous induction, which all 9 anaesthetists have come to prefer. Premedication is with papaveretum, 20 mg., and hyoscine, 0·4 mg., or more commonly with promethazine, 50 mg., and atropine, 0·6 mg. The patient is brought to the anaesthetic room in the position most comfortable for him and an intravenous drip infusion of dextrose is set up. The patient is given oxygen to breathe by mask through a Water's circuit, without the canister, with a flow high enough to prevent unpleasant symptoms of rebreathing. After 3 minutes the nitrogen is held to have been largely washed out of the alveoli, and oxygen, 2 litres per minute, with nitrous oxide, 8 litres per minute, is given. Complete silence is necessary in the anaesthetic room. After breathing this mixture for 2 minutes, or earlier if signs of Stage-II anaesthesia are observed, an apnoeic dose of D–tubocurarine is given intravenously. Respiration is assisted and finally controlled as apnoea supervenes. Intubation is performed with a cuffed tube, the soda-lime canister is inserted into the circuit, and the gas flow reduced. Further doses of D–tubocurarine are given if necessary. Atropine, 1·3 mg., is injected near the end of the operation, and when tachycardia is evident and spontaneous respiration has begun neostigmine, 2·5 to 5 mg., is injected. The soda-lime canister is removed, and anaesthesia maintained with N_2O, 6 litres per minute, and O_2, 2 litres per minute. Pure oxygen is administered immediately after the operation for a short time to avoid diffusion anoxia. *D. D. C. Howat*

781. **The Adrenal Cortical Response to Surgery. I. The Effect of Anaesthesia on Plasma 17-Hydroxycorticosteroid Levels**

R. W. VIRTUE, M. L. HELMREICH, and E. GAINZA. *Surgery* [*Surgery*] **41**, 549–566, April, 1957. 2 figs., 27 refs.

In this study, reported from the University of Colorado School of Medicine, the effect of anaesthesia on the free and glucuronic acid-(conjugated) plasma 17-hydroxycorticosteroid level and on the adrenocortical response to surgery was investigated in 70 patients aged from 5 to 81 years who were divided into four groups as follows: (1) 35 patients in whom, after induction with thiopentone and cyclopropane, cyclopropane alone, or nitrous oxide alone, anaesthesia was maintained on ether; (2) 15 patients given thiopentone and nitrous oxide throughout; (3) 10 patients given cyclopropane only; and (4) 10 patients receiving spinal analgesia (amethocaine). Control blood samples were taken during the morning hours in order to equate the diurnal cycle, and after one hour of inhalation anaesthesia (after 15 to 45 minutes for spinal analgesia); a second sample of blood was taken before the start of the operation. After one hour of surgery a third sample was taken, and the plasma level of free 17-hydroxycorticosteroids estimated by the modified method of Nelson and Samuels. Conjugated 17-hydroxycorticosteroids were determined by Bongiovanni's method, with benzene–water partitioning.

The mean control level of free plasma 17-hydroxycorticosteroids for the entire group was found to be 12·8 μg. per 100 ml. of plasma, a result agreeing well with other reported values. Cyclopropane, thiopentone–nitrous oxide, and spinal analgesia caused no significant rise in the 17-hydroxycorticosteroid level, only 3 out of the 35 patients in these groups showing an appreciable rise. Of the 35 patients maintained on ether, however, 15 showed a significant rise in the mean value, but the effect was quite inconsistent, the other 20 showing only minor changes. Thus of the total 70 patients, 18 showed a

significant increase in the free plasma 17-hydroxycorticosteroid level, and of these 15 had received ether. After the operation had been in progress for one hour the plasma level of free 17-hydroxycorticosteroid rose significantly in the three groups receiving inhalation anaesthesia, but no appreciable change in level occurred in the group given spinal analgesia.

The conjugated plasma hydroxycorticosteroid level was also estimated in 24 patients, 15 of whom received ether. Because a delay in the rise of conjugated plasma levels occurs following a rise in the free plasma level, blood samples were also taken at the end of surgery in these cases. The mean plasma values for both conjugated and free steroids were found to follow identical curves in all three groups given inhalation anaesthesia. These results show the effect of different anaesthetics on the pituitary–adrenocortical system and the authors discuss the significance of their findings. The absence of a rise in plasma hydroxycorticosteroid levels under spinal analgesia demonstrates that intact sensory pathways to the central nervous systems are necessary for the normal adrenocortical response to trauma to appear. Although some workers have reported that barbiturates cause a partial suppression of the adrenocortical response to cold and even to surgical trauma, the different premedication agents used in this study did not appear to affect the subsequent response to anaesthesia and surgery.

Discussing the mechanism by which such rises in plasma steroid levels occur the authors conclude that adrenocortical stimulation rather than a decreased rate of steroid disappearance from the plasma is the factor responsible. *Raymond Vale*

782. **Investigation of Cerebral Damage Following Induced Hypotension**

O. BERG, E. NILSSON, and E. VINNARS. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **29**, 146–150, April, 1957. 3 figs., 15 refs.

Reporting from the University Hospital, Lund, Sweden, the authors state that cerebral damage following induced hypotension has been previously studied mainly in three ways: by cerebral haemodynamic measurement, by electroencephalography (EEG), and by the "psychophysical" flicker-fusion test of Berg. The last-named method was used in this investigation on 73 surgical patients receiving induced hypotension, in 28 of whom a simultaneous EEG was also obtained; the results were compared with those in 30 control patients operated on without hypotension. The Berg method depends on the appreciation of a flickering light of varying frequency or intensity, as continuous light, thus assessing the function of the retino-cortical pathways and cortex. The critical threshold value is uninfluenced by training and is usually constant, showing but little variation for any given individual. The test is improved by giving hexobarbitone in a dose of 50 to 100 mg. according to age and body weight; this has no effect on the critical threshold in normal subjects, but in the presence of diffuse cerebral injury such as encephalitis or cerebral hypoxia it is decreased, and if it remains so for more than 8 minutes the test is said to be positive. If cerebral damage is severe the critical threshold may be lowered for 2 or 3 weeks and then return to normal.

In the patients studied hypotension was induced with either hexamethonium or trimetaphan for periods varying from 20 to 90 minutes. In these the flicker-fusion test was negative in 35 cases and positive in 38, remaining so for more than 6 days in 9 of the latter. The test in all 30 control patients gave a negative result. The series included 35 patients with malignant disease and in these the test was positive about twice as frequently as in the others. There was a higher incidence of positive reactions in males but no difference in age groups above and below 50. Positive tests were equally frequent at blood pressure levels above and below 80 mm. Hg, and the frequency ratio of positive and negative tests in horizontal and head-up positions did not differ, though 7 out of 10 patients with a prolonged positive reaction had systolic pressures below 80 mm. Hg in the head-up position. The frequency of positive tests did not vary with the duration of hypotension. In the 28 cases in which the EEG was also recorded the flicker-fusion test was negative in 11, 9 of whom showed EEG abnormalities. Of 17 with positive flicker-fusion tests, only 9 showed EEG abnormalities. Of 7 patients with a prolonged positive reaction to the test, 3 had a normal EEG.

The authors conclude by suggesting that the flicker-fusion test may be more sensitive than the electroencephalogram [but the disparity suggests that these two investigations may indicate a different site of injury]. *Raymond Vale*

783. **Fluoromar in Anaesthesia**

J. W. DUNDEE. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **50**, 191–193, March, 1957. 8 refs.

The use in anaesthesia of certain halogenated ethers, and particularly trifluoro-ethyl-vinyl ether ("fluoromar"), has been reported since 1953. This preparation is stable and unaffected by contact with hot soda-lime. Although less inflammable than ethyl ether and requiring a stronger spark to ignite it, it is, in fact, still well within range (3 to 8 vol. %) of clinically useful concentrations. It does not sensitize the heart to adrenaline, nor does it cause any more hepatic upset than the other ethers. Its boiling-point of 42·7° C. makes open-drop techniques hardly practicable.

The author, who has used fluoromar for 287 premedicated patients, found that it was less irritant than ethyl ether with a consequently smoother induction, but Guedel's classic signs in relation to stage of anaesthesia were confused and the anaesthesia was so flexible that either the patient could rapidly become apnoeic or the depth inadequate. Good relaxation could be produced, but not as readily as with ethyl ether, and there was the complication of a tachypnoea which increased as the administration continued and could produce a tidal volume so small as to cause a respiratory acidosis. This, together with the fact that it is a relatively poor analgesic, leads the author to conclude that it has insufficient merit to justify its introduction into British anaesthetic practice. *Donald V. Bateman*

Radiology

784. **Cerebral Angiography in Encephalotrigeminal Angiomatosis**

C. M. POSER and J. M. TAVERAS. *Radiology* [*Radiology*] 68, 327–336, March, 1957. 7 figs., 30 refs.

The authors present their conclusions which are based on the results of cerebral angiography in 15 cases of encephalo-trigeminal angiomatosis in patients aged from 5½ months to 18 years examined by them at the Presbyterian Hospital (Columbia University), New York, and on those in 35 additional cases examined by the same procedure reported in the literature.

Angiography by means of serial films revealed a cerebral vascular abnormality in 23 of the 50 cases. In addition to the classic capillary-venous angioma usually observed in this syndrome, there were also arteriovenous malformations, anomalies of the cerebral veins and dural sinuses, and anomalies in the territory of the external carotid circulation. Some cases also showed subdural haematoma, cerebral atrophy, or hypoplasia. Intracranial calcification was seen in the radiograph in 27 cases. It was found that increasing age and the presence of intracranial calcification decreased the chances of demonstrating vascular abnormalities by cerebral angiography.

Follow-up studies in 2 cases revealed a rapid development of massive calcification of the Sturge–Weber type in patients with previously diagnosed capillary-venous angioma. The authors conclude that if an intracranial angioma has been demonstrated by angiography, rapid and massive cortical calcification will probably develop.

A. Orley

785. **Secretory Sialography in Diseases of the Major Salivary Glands**

P. RUBIN and J. F. HOLT. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] 77, 575–598, April, 1957. 17 figs., 42 refs.

The authors describe the technique of sialography as carried out on 100 patients at the University of Michigan, Ann Arbor, and correlate the clinical, pathological, and radiological findings. The salivary duct orifice is first dilated and then a No. 60 polyethylene catheter, containing a fine wire stylus for rigidity, is inserted for a distance of 3 to 4 cm. "Pantopaque" (ethyl idiophenylundecylate), which is considered to be the most satisfactory contrast medium, is then injected slowly and after 0·25 ml. has been given most patients experience a sensation of pressure. The end-point of the injection is when definite pain occurs, that is, usually after the injection of between 0·5 and 1 ml. in normal glands, but up to 2 ml. may be required if there is dilatation of the duct system. The end of the catheter is then plugged with a wooden toothpick and films taken of the filled gland. The ideally injected gland shows filling of the intercalary ducts and minimal delineation of the acini. After sialography the patient sucks a lemon for one minute in order to stimulate the flow of saliva and wash the contrast medium out of the gland. A "post-evacuation film" is taken at 5 minutes, by which time the normal gland is usually free of contrast medium. If, however, acinar filling has occurred, a fine cloud of contrast material outlines the gland in the 5-minute film, but has usually disappeared if a further film is taken at one hour or at the latest at 24 hours.

Sialography is contraindicated in acute inflammatory disease of the gland. Chronic inflammatory swelling can be divided into 2 main categories. (1) Chronic obstructive sialodochiectasis. Salivary calculi are the commonest cause of obstruction; some 20% of submaxillary calculi and 40% of parotid calculi are non-opaque and may show only as a filling defect. Dilatation occurs in the main ducts behind the stone, and during injection of the medium the stone may be forced backward into the dilated duct. In early cases, the peripheral ducts appear normal, but in chronic cases there is loss of the arboreal pattern due to parenchymal atrophy. If secondary infection occurs, sialography may demonstrate irregularly situated small abscess-like cavities. Strictures are a less common cause of obstruction. They may occur at the orifice of the duct or they may be multiple, and they also cause dilatation of the main ducts. In films taken in the secretory phase the functional capacity of the gland can be determined; occasionally a ball-valve mechanism may be demonstrated, resulting in retention of the opaque material distal to the calculus.

(2) In non-obstructive sialodochiectasis, which may occur in Mickulicz's disease, Sjögren's syndrome, or in recurrent pyogenic parotitis in children or adults, the abnormalities are principally situated in the peripheral ducts. Inflammatory changes around the interlobar and interlobular ducts produce stenosis of these ducts, with dilatation of the peripheral intralobular ducts. The earliest sialographic changes are of a diffuse punctate dilatation of the peripheral ducts. In moderately advanced disease there is further dilatation, which produces a mulberry-like pattern of globules. With further advance of the condition these globules coalesce to form irregular cavities. In the final destructive state the sialogram presents a bizarre pattern resembling that of neoplastic invasion. The emptying phase of the gland is slowed owing to narrowing of the interlobular ducts and the secretory pressure may cause the intralobular ducts to dilate further. In the destructive stage the bizarre shadows produced by the contrast medium may remain unchanged for days or weeks because of the absence of secretory tissue.

In cases of neoplastic disease of the salivary glands extrinsic neoplasms may displace the duct system of the gland slightly and crowd the peripheral acini, but the general architecture of the gland is preserved and there

is normal emptying in the secretory phase. Intrinsic non-invasive neoplasms of the salivary gland tend to displace the duct system to a greater extent, but the normal branching pattern is maintained; there may be localized pressure on the larger ducts so that in the secretory phase there is characteristically some retention of contrast medium in some of the peripheral ducts. In contrast, intrinsic invasive neoplasms displace and distort the duct system and the acinar pattern is replaced by a bizarre "puddling and pooling" of the opaque medium owing to destruction of the terminal ducts by neoplastic invasion, so that the medium escapes into the adjacent tissues. When the secretory tissue has been totally destroyed, the bizarre pattern remains unchanged for up to 48 hours. If there is only partial destruction of the secretory tissue, stimulation may cause the contrast medium to pass into the tissues of the gland instead of being washed out in the normal manner. *G. Ansell*

786. **Bronchography with Barium.** (Die Bronchographie mit Barium)
S. DI RIENZO and R. O. PEREIRA DUARTE. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [*Fortschr. Röntgenstr.*] **86**, 315–318, March, 1957. 4 figs.

A viscous barium preparation (barium suspended in carboxylmethyl cellulose) has been used by the authors as a contrast medium for bronchography. The advantages of this non-oily medium over oily preparations and over iodine-containing contrast media suspended in carboxylmethyl cellulose are stressed. The barium contrast medium disappears from the bronchial tree within 72 hours, it is not toxic, and its price is about one-twentieth of that of the usual media for bronchography.
M. E. Grossman

787. **The Roentgenologic Diagnosis of Esophageal Varices**
S. W. NELSON. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **77**, 599–611, April, 1957. 16 figs., 7 refs.

The various factors which are of importance in demonstrating esophageal and gastric varices have been discussed. If the following factors are kept in mind during the study of patients suspected of having esophageal and gastric varices, the highest possible degree of diagnostic accuracy will be attained: (1) Recumbent and Trendelenburg position should be used. (2) Thick barium mixtures are preferable, although various thinner mixtures will often suffice. (3) Carboxymethylcellulose in 0·25–0·75% mixed with ordinary barium mixtures will improve the adherence of the barium to the esophageal and gastric mucosa. (4) Atropine sulfate in doses varying from 0·5 to 1·0 mg. subcutaneously 30 minutes before the examination will also increase the adherency of the barium to the mucosa.

(5) Multiple fluoroscopically controlled spot roentgenograms are necessary in varying positions because smaller varices will often only be shown in one projection. (6) Esophageal peristalsis is very powerful and a peristaltic wave can obliterate the varices. Under fluoroscopic control esophageal relaxation can be observed and the esophagus roentgenographed in a more relaxed state during which the varices usually fill. (7) The Valsalva maneuver properly performed is usually of great value in demonstrating varices, probably because during the sustained Valsalva maneuver (if the patient does not swallow) no further primary peristaltic waves are initiated and the esophagus will eventually relax. (8) Venous pressure will usually increase during the Valsalva maneuver and this, too, is felt to play a role in the visualization of the varices during this maneuver. (9) The phrenic ampulla, if present, can be of great value during the sustained Valsalva maneuver because the pinch-cock effect of the diaphragm can trap barium in the ampulla during the progression of the primary peristaltic wave towards the distal esophagus. If the Valsalva maneuver is sustained, esophageal relaxation will occur and allow small amounts of barium to flow retrograde into the relaxing esophagus and thus demonstrate the varices at an optimum time during their filling. (10) The Valsalva maneuver will frequently prevent the visualization of varices in the lower esophagus because the pinch-cock effect of the diaphragm during the maneuver is felt to prevent filling of the varices from the abdomen. By discontinuing the maneuver for 3 or 4 seconds, the varices may fill and then be properly roentgenographed.

(11) In order to demonstrate varices in the abdominal portion of the esophagus, respiration should be suspended comfortably in the expiratory phase. The Valsalva maneuver will obliterate varices in the abdominal portion of the esophagus. (12) The Müller maneuver will occasionally show varices when all other methods have failed. (13) Too much barium in the esophageal lumen will frequently obscure even large varices. Relief techniques using smaller amounts of barium are much more likely to demonstrate even the smaller varices.

Improving surgical techniques for the alleviation of bleeding from esophageal and gastric varices justify a more diligent approach in demonstrating varices as early as possible in those patients suspected of having them. The author has not discussed the demonstration of esophageal and gastric varices by means of splenoportography. Rather he has limited his discussion to methods and techniques available to all radiologists.—[From the author's summary.]

788. **Carbon Dioxide as Contrast Medium for the Visualization of the Heart and Vessels.** (Kohlendioxyd als Kontrastmittel für die Röntgendarstellung des Herzens und der Gefässe)
F. GROSSE-BROCKHOFF, D. KOCH, F. LOOGEN, G. ROTTHOFF, H. VIETEN, and K. H. WILLMANN. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [*Fortschr. Röntgenstr.*] **86**, 285–291, March, 1957. 5 figs., 16 refs.

After preliminary experiments on pigs the authors have carried out angiocardiography on human subjects using carbon dioxide as contrast medium. No adverse effects have been observed with quantities of gas up to 200 ml. in carefully selected cases. Angiocardiograms

made by this method in 2 illustrative cases, one of isolated stenosis of the pulmonary valve and one of Fallot's tetralogy, are reproduced. *M. E. Grossmann*

789. **The Basis of Pneumoradiography of the Right Heart with Carbon Dioxide.** (Die Grundlagen der Pneumoradiographie des rechten Herzens mit Kohlendioxyd)
W. HÖFFKEN, R. JUNGHANS, and W. ZYLKA. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [*Fortschr. Röntgenstr.*] **86**, 292–301, March, 1957. 5 figs., 17 refs.

A comprehensive account is given of experiments on rats, rabbits, and dogs in which the use of carbon dioxide as a contrast medium for angiocardiography was studied. The authors' findings concerning compatibility, tolerance, dosage, and possible complications are tabulated. [The paper is not illustrated.]

The authors claim that the superior vena cava, the right heart, the various segments of the pulmonary artery, and the pulmonary and mitral valves are well shown by means of this technique. *M. E. Grossman*

790. **Colloidal Stannic Oxide. Animal Studies on a New Hepatolienographic Agent**
H. W. FISCHER. *Radiology* [*Radiology*] **68**, 488–498, April, 1957. 5 figs., 25 refs.

791. **Roentgenographic Evaluation of Coarctation of the Aorta in Infants**
R. G. LESTER, A. R. MARGULIS, and C. M. NICE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 1022–1026, March 23, 1957. 5 figs., 12 refs.

The value of radiology in coarctation of the aorta was studied at the University of Minnesota Medical School, Minneapolis, in 30 cases, in 29 of which operation or necropsy was performed in the first year of life; in the remaining case the condition was diagnosed at the age of 6 weeks but operation was delayed until the age of 4. The classification used was based on the relationship of the ductus or ligamentum arteriosum to the aorta, as follows. Type 1, coarctation distal to the ligamentum or ductus: (*a*) with ligamentum arteriosum; (*b*) with a patent ductus. Type 2, coarctation proximal to the ligamentum or ductus: (*a*) with a patent ductus; (*b*) with a ligamentum arteriosum. The coarctation was of Type 1 in 17 cases and of Type 2 in 13. The condition was diagnosed from both radiological and clinical findings, and the authors stress the importance of two clinical signs—the variation in blood pressure between the upper and lower limbs and the presence of differential cyanosis.

In Type 1 (*a*) there was radiological evidence of enlargement of the left ventricle and left auricle. The pulmonary vasculature was apparently normal. There was also left ventricular and atrial enlargement in Type 1 (*b*), and often enlargement of the right ventricle as well. The most striking feature was a definite increase in the pulmonary vascularity. The authors point out that retrograde aortography will demonstrate simultaneous opacification of the aorta and pulmonary arteries, and may show the ductus.

In the uncomplicated case of Type 2 (*a*) the picture was mainly one of an enlarged right ventricle. The pulmonary vessels might be of normal calibre or show a slight increase in size. There were only 2 cases of Type 2 (*b*) in the series, and in these there was both right- and left-sided cardiac enlargement. Notching of the ribs was not seen in any of the cases. Combined lesions affected the radiological picture. It is emphasized that in many cases clinical and radiological information obtained by conventional means is sufficient to reach a diagnosis; in others it may be necessary to have recourse to retrograde aortography or angiocardiography, or both.

The prognosis is best in cases of Type 1 (*b*), 5 out of 8 of these patients with this type of coarctation surviving operation. *L. G. Blair*

792. **Venography in Superior Vena Caval Obstruction**
G. W. HUDSON. *Radiology* [*Radiology*] **68**, 499–506, April, 1957. 3 figs., 19 refs.

793. **Roentgen Manifestations of Psoriatic Arthritis**
T. F. MEANEY and R. A. HAYS. *Radiology* [*Radiology*] **68**, 403–407, March, 1957. 6 figs., 15 refs.

Arthritis has long been recognized as a complication of psoriasis, and since this latter condition is not infrequently associated with rheumatoid arthritis the question has arisen whether the joint changes are entirely due to the associated condition or whether psoriatic arthritis is itself a disease entity. The authors of this paper from the Cleveland Clinic, Ohio, review the literature, and on the basis of the radiological findings in the hands of 15 patients with psoriasis and arthritis suggest that such patients may be divided into two groups. [Unfortunately, no reference is made to the incidence of skeletal involvement when all cases of skin affection are included.]

In the larger group (11 cases) the usual radiological manifestations of rheumatoid arthritis were clearly present—generalized demineralization of bone, narrowing of the joint spaces, erosion of articular surfaces, and soft-tissue swelling around the affected joints. [One illustration also shows early ulnar deviation of the fingers.] The significant features in these cases were the generalized nature of the bone changes and particular involvement of the proximal interphalangeal joints. Parallelism between the psoriasis and the arthritis, or the simultaneous waxing and waning of symptoms of both conditions, led the authors to conclude that psoriasis acts as a non-specific stimulus for the exacerbation of an existing arthritis, particularly arthritis of the rheumatoid type. The remaining 4 cases were true cases of psoriatic arthritis with different radiological features. No generalized demineralization of bone was seen, and destruction was noted in one or more distal interphalangeal joints, with little or no change in the proximal joints. This destruction was articular in type, leading later to fibrous or bony ankylosis, but some hypertrophic change was also seen around the margins of the affected joints. There was a tendency to psoriatic involvement of the finger nails in those digits where underlying arthritic changes of this type were present. *R. O. Murray*

RADIOTHERAPY

794. **Planned Combination of Surgery and Radiation in Treatment of Advanced Primary Head and Neck Cancers**
W. S. MacComb and G. H. Fletcher. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] 77, 397–414, March, 1957. 11 figs.

It has in the past been considered inadvisable to use surgery after irradiation because of the danger of delayed healing, necrosis, and haemorrhage. Similarly, radiotherapy has been regarded as unacceptable after surgery because the diminished blood supply due to scar-tissue formation decreases radiosensitivity. Tumours of the head and neck—because recurrence is frequent after primary treatment and because neither of these methods can be successfully employed a second time—offer an opportunity to increase the " salvage rate " by using both methods together. This has been done at the University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas, in a systematic planned programme extending over 5 years, for tumours of the nasal sinuses, the oral cavity, oropharynx, extrinsic larynx, and parotid region, which sites appear to have satisfactory tolerance to consecutive radical procedures. In the paranasal sinuses surgery precedes intracavity or external irradiation. In tumour of the oral cavity and oropharynx irradiation is employed first, and surgery later for metastatic residual or recurrent disease. In advanced tumours of the pyriform sinuses pan-laryngectomy with block dissection of the neck is done; external irradiation is then given to the entire area, and this at times is supplemented with radium implantation. For parotid tumours excision and block dissection precede radium implantation or radioactive cobalt therapy. It is suggested that supervoltage therapy has definite advantages in this combined treatment because of the ease of treatment, the increased tolerance to irradiation, and lessened postoperative difficulties, especially as regards wound healing. A number of case reports illustrate the results of such combined treatment. *I. G. Williams*

795. **Management of Advanced Breast Carcinoma. With Special Reference to Combined Radiation and Hormone Therapy**
F. C. H. Chu, D. W. Sved, G. C. Escher, J. J. Nickson, and R. Phillips. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] 77, 438–447, March, 1957. 31 refs.

Over 4 years ago a programme was instituted at the Memorial Hospital, New York, to determine the relative benefits and possible synergism of combined hormone and radiation therapy, as compared with either alone, in the treatment of inoperable, recurrent, and metastatic cancer of the breast. A review of the literature shows that patients with metastases from breast cancer treated with radiation therapy live longer than those untreated (20 months as against 8 months in one series of 83 cases). With hormone therapy it is reported that patients who respond live about twice as long as those who do not respond.

In the present series of 58 cases, those patients with inoperable disease localized to the breast and regional nodes or with one single metastatic site were treated by irradiation, while those with more advanced or widespread disease were treated both by radiation and with steroids. For the latter group, wherever possible, patients with bilateral comparable disease were sought out, so that one side could be treated by both methods, leaving the lesions on the other side treated with hormones alone for comparison. Patients less than 10 years postmenopausal received androgens and older patients oestrogens for so long as regression was maintained or no progression occurred.

Radiation therapy to the breast and regional lymph nodes was with 1,000-kV *x* rays, a tissue dose of 4,000 to 6,000 r being given in 4 to 6 weeks. For local recurrent disease 1,000- or 250-kV *x* rays in similar dosages. For lymph nodes 250-kV *x* rays were used, 3,000 to 3,500 r being given in 2 to 3 weeks. For scattered skin metastases contact or 100-kV *x* rays were used. Mediastinal, pulmonary, and osseous metastases were treated with 2,000- or 250-kV *x* rays, fractionated therapy being given to a dose of 2,000 r in 2 weeks. The number of lesions treated with radiation alone was 23 and with steroids alone 92, while 35 lesions received combined treatment. The response was evaluated on the basis of objective change in particular lesions.

It was concluded that radiation therapy is an effective palliative in primary carcinoma of the breast and its metastases, the percentage improvement of individual lesions being higher than with steroids alone. The addition of steroid therapy did not appear to detract from or to enhance the radiation response, the effect of combined therapy being what one would expect from irradiation alone. The survival times in comparable groups treated by combined therapy and with hormones alone showed no significant difference. In patients with widespread metastases in whom steroid therapy is indicated, the additional use of irradiation is advisable for the prompt and effective control of individual symptomatic or potentially dangerous lesions, such as bone metastases or ulcerating neoplasms. *I. G. Williams*

796. **The Treatment of Recurrent Carcinoma of the Rectum by Supervoltage *X*-ray Therapy**
I. G. Williams, I. M. Shulman, and I. P. Todd. *British Journal of Surgery* [*Brit. J. Surg.*] 44, 506–508, March, 1957. 3 refs.

An account is given of the treatment of 82 cases of local recurrence of carcinoma of the rectum after surgical excision, *x* rays generated at 1,000,000 volts being used. The advantages of this high voltage are emphasized. In those cases in which the local recurrence was small, a radical cure was attempted, and 6,000 r was given in 6 weeks. When the recurrence was more advanced treatment was purely palliative, 3,000 to 4,000 r being given in 3 to 4 weeks. Of the 82 patients in the series 71 benefited, symptoms being relieved for an average period of 7·7 months. Side-effects were few and slight. In the authors' view the results justify this treatment in all cases of local recurrence after excision of carcinoma of the rectum. *E. Stanley Lee*

History of Medicine

797. **Young Montgomery and His Beating Heart**
H. R. VIETS. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 702–703, April 11, 1957.

Attention is drawn to a little known and unusual clinical description by William Harvey in *Exercitationes de Generatione Animalium* (1651) of a youth who survived an accident in which he lost part of the anterior portion of the chest and whose heart could be seen in action and even palpated. The author of the present paper quotes the full case history from the English translation of the work (1653). The young man, son and heir of the Viscount Montgomery, suffered a fracture of the ribs on the left side when a child. Suppuration set in " for want of the help of a skilfull Physitian ", and part of the chest wall covering the heart sloughed off leaving a vast hole in the breast. Harvey, when he met the youth then aged 18, saw a " fleshy part sticking out of this thoracic defect ", and was amazed to find that this object was indeed the heart, although it had been mistaken by others for a lobe of the lung. For protection a plate was worn over the defect, and " the Young Gentlemans Man did by dayly warm injections deliver that fleshy accretion from the filth and pollutions which grew about it, and so clapt on the Plate: which was no sooner done, but his Master was well, and ready for any journey or exercise, living a pleasant and secure life ".

King Charles I examined the patient with Harvey, and both noticed that the heart was insensitive to the touch of the examining fingers. " We likewise took notice of the motion of his Heart; namely, that in the Diastole it was drawn in and retracted, and in the Systole came forth, and was thrust out; and that the Systole was made in the heart, when the Diastole was sensible in the wrest; and also that the proper motion of the heart is the Systole; and lastly, that the heart then beats upon the breast, and is a little prominent, when it is lifted upwards and contracted into it self."

Harvey's description is also to be found in the unique *Leçons sur la physiologie et l'anatomie comparée de l'homme et des animaux faites à la Faculté des Sciences de Paris* (1857–1881) by Henri Milne Edwards, a series of 14 volumes, which, the author states, are a mine of information on all sorts of matters related to medicine and well worth dipping into, especially by those interested in the heart and circulation.

Montgomery died suddenly when he was 40, but not before he had fought as a Royalist in the Civil War, been honoured by Charles II, married twice, and fathered two sons. *H. P. Tait*

798. **John Mitchell, Benjamin Rush, and Yellow Fever**
S. JARCHO. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **31**, 132–136, March–April, 1957. Bibliography.

799. **Theodore Billroth and the Beginning of Gastric Surgery**
I. MENDELBAUM. *Journal of the Mount Sinai Hospital* [*J. Mt Sinai Hosp.*] **24**, 112–122, March–April, 1957. 2 figs., 27 refs.

Theodor Billroth's life (1829–1894) was contemporaneous with that of Lister (1827–1912), and while Billroth achieved his brilliant surgical technique before adopting Lister's theories, of which he was at first critical, the range of his surgery was greatly extended when he accepted Lister's views.

Early in life Billroth showed considerable musical ability and was only deterred from a career in music by the influence of his mother. He studied in Göttingen, and in 1851 went to von Langenbeck's Clinic in Berlin where he remained as an assistant for 9 years. In 1860 he accepted the Chair of Surgery at Zürich, and here he introduced the method of rectal temperature measurement in postoperative patients. He founded the *Archiv für klinische Chirurgie*, and emphasized the need for detailed records and statistical analysis of cases. It was in Zürich that he met Johannes Brahms and a lifelong friendship began. As a relaxation Billroth played in a string quartet with three other professors of the University, and although he was himself a pianist, he learned to play the viola in order to take part.

Billroth's reputation rests on his advances in surgical technique and the establishment of partial gastrectomy as an effective procedure. The latter operation was first carried out by Billroth in 1881 in Vienna. The duodenal anastomosis was made at the level of the lesser curvature, thus producing a pouch below the anastomosis in which food accumulated. Experience suggested that a lower anastomosis on the greater curvature would be more effective, and thus the Billroth-I operation was completed. In 1885, having resected so much of the stomach that it could not be united with the duodenum, Billroth anastomosed the stomach and jejunum, performing for the first time the operation which came to be known as Billroth II.

Among the surgical procedures which he introduced were total laryngectomy, resection of the upper part of the oesophagus, excision of the rectum for carcinoma, and radical mastectomy. Billroth combined breadth of mind and untiring energy with a complete lack of vanity, qualities which endeared him to all with whom he came in contact. He had the devotion of a large number of surgeons, who carried his principles and practice to all corners of the world and established Vienna as the leading school of surgery in the latter half of the nineteenth century. *J. G. Bonnin*

800. **Sir Victor Horsley, 1857–1916. Centenary Lecture**
G. JEFFERSON. *British Medical Journal* [*Brit. med. J.*] **1**, 903–910, April 20, 1957. 5 figs., 31 refs.